



MARCH 2015

THE 2014 DRUG TREND REPORT

THE EXPRESS SCRIPTS LAB™

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INTRODUCTION



COMMERCIALLY INSURED YEAR IN REVIEW

2014 DRUG TREND REQUIRES UNPRECEDENTED ALIGNMENT AND ACTION

For nearly three decades, Express Scripts has delivered innovative solutions that have helped contain rising medication costs for our clients and members. Annual drug spending increases have often been below the annual rate of overall healthcare inflation in the U.S. Throughout this period, achieving the industry's lowest drug trend while still maintaining patient safety – as Express Scripts has done time and time again – has been neither accidental nor easy. Rather, it was the intentional result of our clients taking action and joining us as partners. The aggregate effect of our collective partnership has been to make the use of prescription drugs safer and more affordable.

In 2014, the pharmacy landscape underwent a seismic change, confronting healthcare payers with the highest annual increase in drug spend since 2003. New treatments for nonorphan conditions like hepatitis C were introduced in the U.S. market at exorbitant, orphan-drug pricing. Compounding pharmacies began exploiting a loophole in a new regulation that made the creation and dispensing of unproven topical creams a lucrative cottage industry. Drug manufacturers – brand and generic alike – continued to consolidate, placing additional strain on the supply chain to handle temporary shortages. The pipeline of new medications to treat conditions like cancer and high blood cholesterol also threatened to undermine the sustainability of the U.S. pharmacy benefit.

These challenges are unprecedented, and the need to respond has never been greater. However, plan sponsors can no longer rely on the wave of less-expensive generics to control drug costs. They need to act now to more tightly manage the benefit, implement smarter formularies, control the use of compounded medications and offer clinical support to ensure that all patients are able to achieve the best health outcome possible.

To sustain a meaningful pharmacy benefit, payers must team with a pharmacy benefit manager (PBM) with the strength and scale to challenge the status quo, the flexibility and thoughtfulness to adapt to the evolving marketplace, the curiosity to explore new solutions, and the drive to make pharmacy care in America smarter. Express Scripts is dedicated to expanding both access and affordability, so that every patient receives the right medicine at the right time and at a fair cost. We are prepared to lead and make a difference.

The aggregate effect of our collective **partnership** with clients has been to make the use of prescription drugs safer and more affordable.

DYNAMIC, COMPLEX PHARMACY CHALLENGES LOOM LARGE

The challenges facing plan sponsors include the pipeline of niche drugs, orphan-drug pricing for nonorphan drugs, new innovations in commonly used therapy classes, cost inflation for compounded medications and industry consolidation.

Pipeline of Niche Drugs

Historically, drug manufacturers' business models focused on research and development of key drugs to treat common conditions that affected millions of patients. These branded medications became blockbusters because of the volume of patients treated and a high, but not exorbitant, price tag. As a result of patent expirations, generic competition and a withering pipeline of broad-reaching drugs, manufacturers are shifting their drug discovery, development and pricing strategies. Now, manufacturers are increasing their focus on medications that treat small subsets of patients with diseases like cancer, or patients with rare diseases such as hereditary angioedema.¹

Manufacturers also are tailoring molecular drugs to patients with specific genetic profiles known to be affected by certain diseases, so the drugs are more effective in treating those specific patients. For example, Ruconest® (C1 esterase inhibitor [recombinant]), approved in July 2014, treats adult and adolescent patients with hereditary angioedema, a condition that affects fewer than 10,000 Americans. Another such drug, Cerdelga™ (eliglustat), offers an oral alternative to enzyme replacement therapy for adult patients with Gaucher disease type 1, an inherited lysosomal storage disorder that affects approximately 6,000 patients in the U.S.

In addition, more than 1,000 targeted cancer treatments, many genetically guided, are in development. One such niche cancer drug that recently received approval is Keytruda® (pembrolizumab), an immunotherapy approved in September 2014 to treat a small subpopulation of patients with certain genetic expressions of advanced, non-small cell lung cancer. Keytruda and other niche drugs have the potential to vastly improve outcomes and are often clinical game changers. They typically have little or no competition and are often much more effective than the broader-spectrum drugs they are replacing as first-line or second-line treatments. Many come with unprecedented price tags, however, as pharmaceutical companies try to maintain profit margins and recoup their investments in drug discovery.

To sustain a meaningful pharmacy benefit, payers must team with a PBM with the strength and scale to challenge the status quo, the flexibility and thoughtfulness to adapt to the marketplace, the curiosity to explore new solutions, and the drive to make pharmacy care in America smarter.

Orphan-Drug Pricing for Nonorphan Drugs

Orphan drugs are among the most expensive medications in the U.S., often costing tens of thousands of dollars per prescription. These medications treat extremely rare conditions and diseases with very small, very specific populations – typically only several thousand patients or fewer. The high price tag is necessary – and justified – to fund manufacturer research and development costs for these and future medical breakthroughs that might not otherwise happen.

One example, approved by the U.S. Food and Drug Administration (FDA) in late 2014, is Harvoni® (ledipasvir/sofosbuvir), which is indicated for patients with genotype 1 of the hepatitis C virus. In the U.S. alone, there are an estimated three million patients with hepatitis C – far beyond the 200,000-patient threshold that the FDA uses pursuant to the 1983 U.S. Orphan Drug Act – to qualify an orphan-disease population.² Despite its potential to treat millions of patients, Harvoni is priced at a staggering wholesale acquisition cost of \$1,125 per tablet – more than \$33,000 per 30-day prescription.

These new treatments for hepatitis C are just one example of nonorphan drugs with orphan-drug price tags. Rewarding pharmaceutical breakthroughs is undeniably important to the discovery of future treatments and cures; however, payers and patients have limited resources and simply cannot afford these prices. Absent more fair drug pricing, payers will face half a trillion dollars in prescription drug costs as soon as 2020.



New Innovations in Commonly Used Therapy Classes

Despite the recent focus on the development and promotion of specialty medications, there is still a considerable drug market for medications indicated to treat more common chronic conditions, such as diabetes and high blood cholesterol, which combined affect at least 19 million Americans.³ Although both chronic conditions have well-established treatment regimens, many of which have generic equivalents, recent approvals and innovative pipelines will increase current and future drug spend.



Diabetes medications were the only nonspecialty therapy class to have a significant increase in per-member-per-year (PMPY) drug spend in 2014, largely due to two newly approved medications known as sodium-glucose co-transporter 2 (SGLT2) inhibitors. SGLT2 inhibitors work with the body's natural processes to remove excess glucose from the bloodstream. The FDA approved the first SGLT2 inhibitor in 2013, two more were approved in 2014 and many more are in the development pipeline.

The diabetes pipeline also includes once-weekly oral and injectable treatments that demonstrate greater clinical efficacy than currently available therapies, as well as drugs with new mechanisms of action aimed at regenerating insulin-producing cells.⁴ In addition, we anticipate insulin medications such as Lantus® (insulin glargine) will soon compete with next-generation biosimilar insulins from several pharmaceutical manufacturers, likely spurring the escalation of costs for insulin medications that occurred in 2014.

Diabetes medications were the only nonspecialty therapy class (aside from compounded medications) to have a significant increase in PMPY spend. We anticipate that insulin medications such as Lantus® (insulin glargine) will soon compete with next-generation biosimilar insulins from several pharmaceutical manufacturers.

High blood cholesterol – a therapy class currently dominated by low-cost generics – also is poised for significant cost increases in the coming years. New medications that inhibit proprotein convertase subtilisin/kexin type 9 enzyme, known as PCSK9 inhibitors, are currently in development with a primary indication for the treatment of a genetic disorder called familial hypercholesterolemia. This inherited condition leaves the body unable to remove low-density lipoprotein (LDL) cholesterol from circulation, causing cardiovascular disease to develop early in life.

These new biologic products inhibiting PCSK9 represent a novel way to lower cholesterol and may offer additional treatment options for those patients with very high LDL cholesterol levels. Although PCSK9 inhibitors may initially be used in patients with familial hypercholesterolemia and in those who cannot tolerate statins, their potential for expanded uses as adjunct therapies to lower LDL in general could impact drug spend significantly. Projected to command an annual cost of \$10,000 or more per patient, they eventually could be used as a chronic therapy for a large portion of the 71 million patients in the U.S. with high cholesterol.⁵

Cost of Inflation for Compounded Ingredients

In 2013 and 2014, spend for compound medications escalated rapidly. Compounded drugs now rank as the third-most-expensive therapy class on a PMPY basis, displacing high blood pressure medications, which had ranked among the top three most-expensive traditional therapy classes for at least a decade. Compounding was the primary manner in which prescriptions were prepared until the 1950s, but mass pharmaceutical production had supplanted this method by the 1970s. The volume of compounded prescriptions continued to drop over time, representing less than 1% of all prescriptions by the early 2000s,⁶ and their share is similar today.

The reasons for the current increases in the cost and utilization of compounded medications are complex. Key factors include changes in industry practices that make it easier to track the costs of these medications, marketing and billing practices of compounding pharmacies, physician prescribing and patient demand. Compounding practices are regulated under the Food and Drug Administration Modernization Act of 1997 (FDAMA).⁷ Drug compounders are not required, however, to demonstrate the safety, efficacy, strength, quality or purity of their products – as producers of commercially manufactured drugs must do. Moreover, pharmacies are not required to report compounding-related adverse events to the FDA or, as currently required in only a few states, to the state boards of pharmacy.⁸

An effort toward increased transparency, in fact, began fueling the current increase in trend for compounded medications. In 2012, an updated version of the Health Insurance Portability and Accountability Act (HIPAA) standard for pharmacy claims transactions – National Council of Prescription Drug Plans (NCPDP) Telecommunications Standard Version D.0 – was implemented. One component of this standard was the requirement that all components of compounded drugs be specified and billed using average wholesale price (AWP) at the ingredient level, rather than being rolled up under the highest-priced ingredient according to previous claims and billing standards.⁹ Since then, bulk manufacturers and compounding pharmacies have substantially raised AWP prices for the components of many compounded drugs, creating unsustainable cost increases.

Industry Consolidation

The wave of billions of dollars' worth of brand blockbuster medications losing patent protection in the past few years has led to unprecedented availability of generic drugs, while the resulting competition among manufacturers and suppliers of new generic medications drove down drug costs substantially in most of the top therapy classes. But, the pace of price reductions has begun to slow: generic prices for the most commonly used drugs decreased 20% from 2013 to 2014, compared to the 30% drop seen from 2012 to 2013. And some generic drugs, for example, doxycycline and oxycodone, available generically for many years, experienced considerable price increases in 2014.

The most significant contributing factor was consolidation in the supply chain as a result of merger and acquisition activity among pharmaceutical manufacturers and drug distributors. Fewer manufacturers means less competition and increased prices. There now is only one – or at most, two – generic manufacturers of some specific products, for example, digoxin, when there used to be five or six producing a medication. According to analysts, just three generic drug companies were responsible for almost half of the revenue generated by all generic drugs in 2013.¹⁰ This industry consolidation will continue to be a challenge for payers; but the good news is that, on the whole, generic medications continue to deliver significant cost savings.

INNOVATIVE HEALTHCARE SOLUTIONS DRIVE BETTER HEALTH AND FINANCIAL OUTCOMES

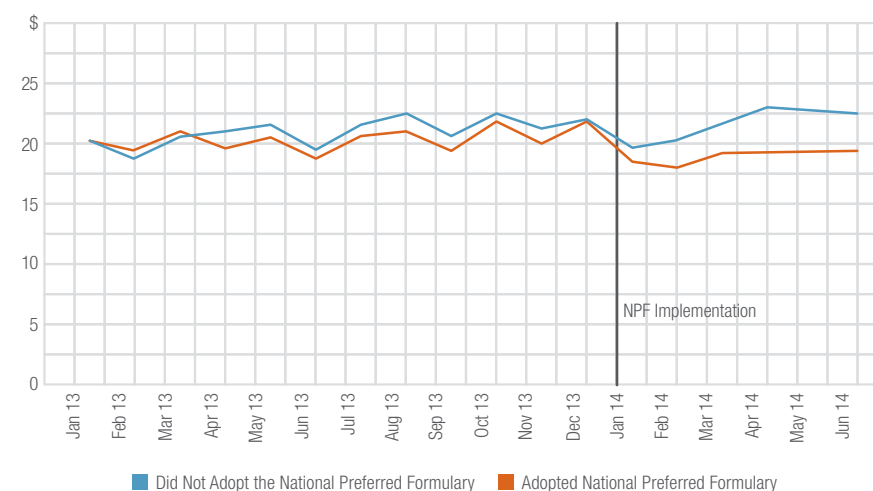
Through the technology and talent at work in the Express Scripts Lab, expanded in 2014, we turn data into insights and insights into proven solutions at an even faster pace. We study, in real time, how patients interact with their healthcare providers and their medications. Using these insights, we rapidly translate research findings into practical applications and proven solutions that address our members' and plan sponsors' most pressing needs. By keeping our clients and members at the center of everything we do, we align our interests to make the use of prescription medications safer, more affordable and more accessible.

National Preferred Formulary

Today, most therapy classes offer more drug choices than ever. But the downside of today's pharmacy climate is that many prescription drugs cost more but deliver no additional health benefit. Smart formulary management is therefore vital to preserve patient access and choice while ensuring that payers can obtain fair and affordable pricing. By excluding a group of “me-too” products from the Express Scripts National Preferred Formulary (NPF),

PLAN COST FOR IMPACTED DRUGS FOR CLIENTS WHO DID AND DID NOT ADOPT THE NATIONAL PREFERRED FORMULARY IN 2014

PMPM PLAN COST FOR IMPACTED DRUGS BY MONTH



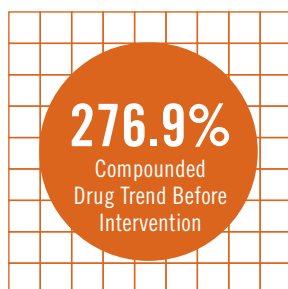
we have the necessary leverage to negotiate more effectively with manufacturers and ultimately achieve lower drug prices for our clients and patients. And in the rare instance when a patient has a medical need for an off-formulary drug, we have a pathway for the excluded drug to be covered for the patient.

In January 2014, we moved 48 products to “not covered” status for our 2014 NPF, which is the selected formulary for approximately 30% of our members. The products that we removed represented only about 1% of all the products currently on our formulary, and were used by fewer than 3% of our members. Importantly, each of these products had clinically equivalent alternatives on the market that remain on our formulary. This effort at cost control without sacrificing patient health paid off for plan sponsors who adopted the 2014 NPF: drug costs in the affected therapy classes decreased on average 3.9% over the same time period in 2013 (see chart on previous page). Among plan sponsors who didn’t adopt the new standards, however, drug costs in the same therapy classes increased on average 7.2% over the first 6 months of 2013.

Our 2015 NPF excludes only 74 drugs out of 4,800 that were available on the market on the first day of the year. As a group, plan sponsors who adopt the 2015 NPF will save more than \$1 billion for the year. In the U.S. healthcare industry – where government does not set price limits on medications and consumers are not exposed to the full price of those medications – smart formulary management is one of the few ways to swing the balance of power from pharmaceutical manufacturers to those who pay for healthcare: health plans, employers, taxpayers and individual patients.

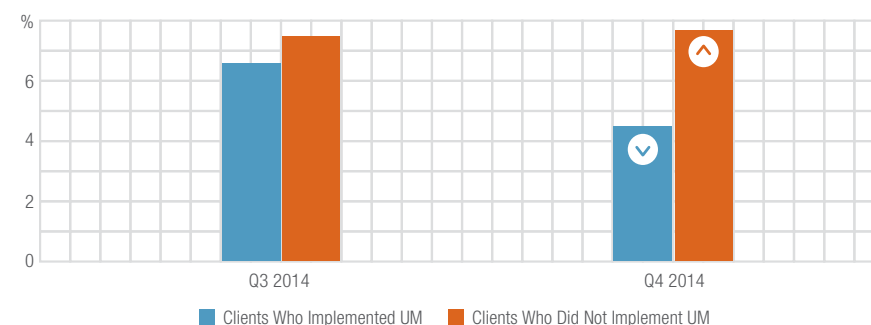
Compounded Drugs

Compounded drugs often cost more than similar FDA-approved medications, but are not necessarily more effective. In response to skyrocketing plan costs for compounded drugs, Express Scripts developed a comprehensive compound-management solution that evaluates all ingredients used in compounded drugs to identify needless cost and waste, actively manages the use of compounded drugs and blocks more than 1,000 clinically unproven ingredients. This solution had a significant and immediate impact on drug spend in 2014. For the first eight months of the year,



COMPARISON OF TRADITIONAL DRUG TREND IN CLIENTS WHO DID AND DID NOT IMPLEMENT OUR COMPOUNDED DRUG UTILIZATION MANAGEMENT (UM) SOLUTION

IN 2014



before the compound-management solution was offered, plan sponsor spend for compounded medications was 276.9% greater than spend for the same period in 2013. By contrast, after the four-month period post implementation of the compound-management solution, the growth in plan sponsor spend had slowed to 128.4%.

The chart above shows the solution’s monthly impact by comparing the traditional drug trend for commercial plan sponsors that chose to actively manage compounded drugs and the trend for those that did not. In September, the traditional trend for the sponsors that began actively managing compounded-drug spend was 6.6%, compared to a trend of 7.5% for plan sponsors that were either waiting to implement the program or did not intend to implement the program.

Compounded-drug spend continued to decrease among clients that were actively managing their spend for these drugs. By December 2014, the traditional trend for clients who had implemented the management solution was 4.5%, a decrease of 2.1 percentage points over the four-month period, while it was 7.7% for clients who had not. By continuously monitoring for clinically unproven ingredients used in compounded medications, the solution has eliminated the majority of unnecessary spend for these medications with minimal patient impact.

Actions to Establish More Fair Drug Pricing

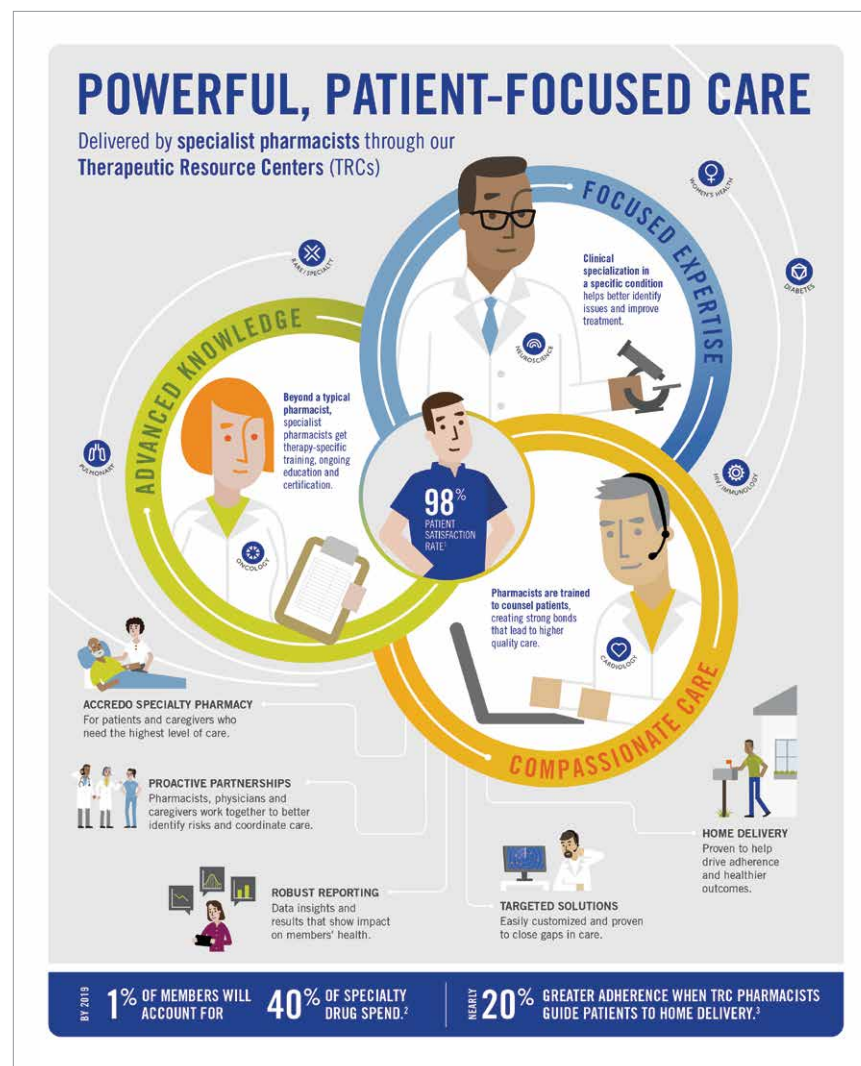
Throughout 2014, Express Scripts was largely critical of a recent trend of drug manufacturers: bringing products to market that, while innovative, are priced so high that payers could not sustain the burden. The leading example was the hepatitis C treatment Sovaldi® (sofosbuvir), whose cost of \$84,000 threatened to bankrupt both private and public plan sponsors around the United States. Never before had a drug to treat a population so large been priced so high. Clients and patients needed a champion, and Express Scripts took action.

After a year-long campaign advocating for more fair drug pricing, Express Scripts announced in December a new agreement with AbbVie, makers of the new hepatitis C medication Viekira Pak™ (ombitasvir/paritaprevir/ritonavir packaged with dasabuvir). The unprecedented arrangement addresses both affordability for payers and access for patients. The cost to cure is now low enough that plan sponsors can afford to treat all hepatitis C patients with genotype 1, not just the sickest.

Therapeutic Resource Centers

The clinically specialized Therapeutic Resource Centers (TRCs) of the Express Scripts PharmacySM and Accredo Specialty Pharmacies deliver superior treatment outcomes and cost-effectiveness by supporting patients through the challenges of complex and costly diseases. Our specialist pharmacists and nurses each receive clinically specialized training in one disease state, and the work they do focuses almost exclusively on that clinical condition. This specialized expertise and commitment enables an optimal patient experience and ensures the highest performance in pharmacy safety, improved medication adherence and closing gaps in care. With their highly specialized knowledge of the complex disease states and complicated treatment protocols they manage, these TRC pharmacists and nurses often have more experience in rare conditions than some of the physicians who prescribe the treatments. For example, the Multiple Sclerosis (MS) Therapeutic Resource Center® manages 72,000 patients with MS, whereas the typical neurologist might have only a few MS patients in his or her entire practice.

TRCs are responsible for interacting with millions of members each year, and each interaction is an opportunity to provide expert clinical counseling, reconcile a drug safety issue or close a gap in care. Annually, the TRCs are involved in over 30 million clinical interactions and close more than 4.8 million gaps in care. Accredo's Hepatitis Therapeutic Resource Center®



delivers the industry's highest level of successful therapy completion, which is critical to a patient's avoiding future virus resistance. In addition, Express Scripts research suggests that patients who received care through the Express Scripts Therapeutic Resource Centers had between 11% and 19% better adherence to oral diabetes, hypertension and statin medications than patients at even the highest-performing retail pharmacies.¹¹

Managed vs. Unmanaged Clients

Balancing patient access and costs is a challenge for every payer, given the volume of therapeutic options available and the variety of conditions those medications treat. Leveraging decades of clinical experience and innovation, Express Scripts' research-driven, state-of-the-art clinical programs and management solutions help optimize drug utilization and costs.

We examined the impact of multiple utilization-management and cost-management strategies on traditional drug spend in 2014.¹² Strategies such as drug tier levels, step therapy programs, out-of-pocket pay differentials, formulary management and utilization of home delivery from the Express Scripts Pharmacy were considered. In the study, plan sponsors were categorized into one of three groups based on the type of network-management and utilization-management programs they implemented as part of the pharmacy benefit:

- Unmanaged — Plan sponsors who did not implement any, or who implemented only one utilization-management or cost-management program
- Managed — Plan sponsors who implemented two or three of the five network-management or utilization-management programs offered
- Tightly managed — Plan sponsors who implemented four or five of the network-management or utilization-management programs offered

The results showed that “unmanaged” plans experienced an annual average increase in PMPY spend for traditional medications of 4.1% in 2014, whereas “tightly managed” plans' traditional drug spend increased only 0.3%. Compared to unmanaged plans, tightly managed plans spent 27.6% less on traditional drugs per member in 2014.

Compared to unmanaged plans, tightly managed plans spent **27.6%** less on traditional drugs per member in 2014.

A LOOK AT OVERALL DRUG TREND FOR 2014

Overall drug spend increased 13.1% in 2014, following several years of declining rate increases. Market forces and changes in patient behavior impacted drug expenditures in 2014, but brand drug cost was one of the most important factors driving trend, especially for specialty medications.

Drug trend comprises two main components: utilization and unit cost. The utilization of traditional prescription medications decreased marginally (0.1%) from 2013 to 2014, but the use of specialty medications increased 5.8%. Unit costs – the costs of the medications themselves – drove spending for both traditional and specialty medications higher by 6.5% and 25.2%, respectively. The 13.1% overall trend was composed of a 6.4% increase in spend for traditional (nonspecialty) medications and a 30.9% increase in spend for specialty medications, the highest specialty drug trend ever recorded. Specialty medications continued to contribute an ever-increasing share of total spend (31.8%, up from 27.7% in 2013) that is expected to reach 44% in the next three years. (Note: Roughly half of specialty medication drug costs are billed through the medical benefit and therefore are not included in our trend calculation.)

COMMERCIALLY INSURED: COMPONENTS OF TREND

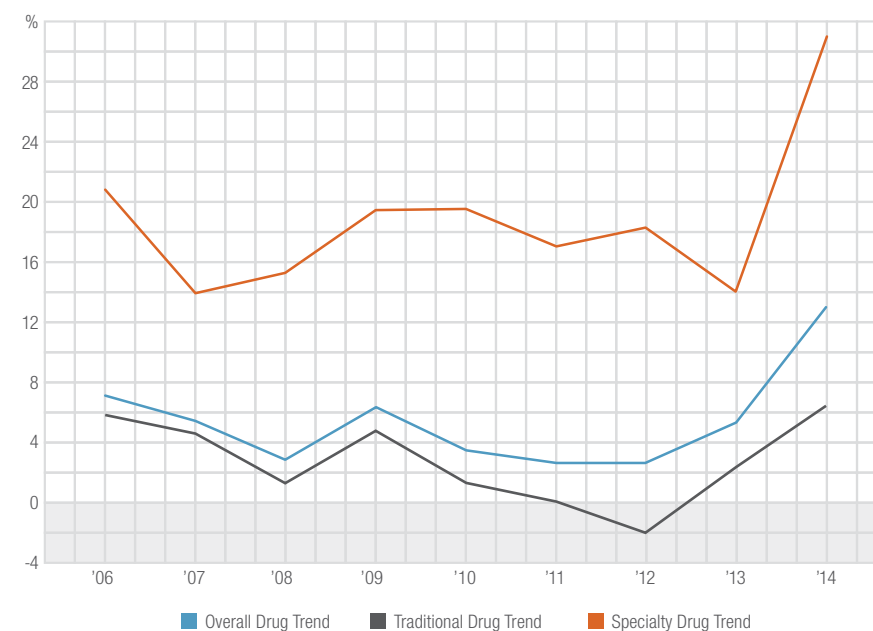
2014

	PMPY SPEND	TREND		
		UTILIZATION	UNIT COST	TOTAL
Traditional	\$668.75	-0.1%	6.5%	6.4%
Specialty	\$311.11	5.8%	25.2%	30.9%
TOTAL OVERALL	\$979.86	-0.04%	13.2%	13.1%

January-December 2014 compared to same period in 2013

TRADITIONAL, SPECIALTY AND OVERALL TREND

2006 TO 2014





THERAPY CLASS REVIEW



COMMERCIALLY INSURED: TRADITIONAL THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Diabetes	\$97.68	1.7%	16.3%	18.0%
2	High Blood Cholesterol	\$48.73	-2.9%	-3.9%	-6.8%
3	Compounded Drugs	\$46.04	0.2%	128.2%	128.4%
4	Pain/Inflammation	\$45.98	0.3%	15.7%	16.0%
5	High Blood Pressure/Heart Disease	\$36.06	-0.4%	-12.2%	-12.6%
6	Heartburn/Ulcer Disease	\$33.40	-1.4%	-9.2%	-10.6%
7	Asthma	\$29.59	-3.2%	-11.6%	-14.9%
8	Attention Disorders	\$27.97	3.4%	2.9%	6.3%
9	Depression	\$25.98	2.1%	-20.5%	-18.4%
10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

For the fourth consecutive year, medications used to treat diabetes were the most expensive traditional therapy class when ranked by per-member-per-year (PMPY) spend. Additionally, the diabetes class had the largest trend with the exception of compounded drugs – which jumped into third place – largely due to a 128.2% unit cost trend. Total trend was negative for half of the top 10 therapy classes (high blood cholesterol, high blood pressure/heart disease, heartburn/ulcer disease, asthma and depression), stemming from declines in utilization, unit cost or both among the different classes.

The top three therapy classes (diabetes, high blood cholesterol and compounded drugs) contributed 28.8% of traditional drug spend in 2014. Although high blood cholesterol drugs

remained among the top three therapy classes, high blood pressure medications dropped from number three to number five as compounded drugs rose in rank to the third most expensive therapy class and pain/inflammation moved up from number nine to number four.

Utilization, which increased less than 1.0% in two of the top 10 traditional classes (compounded drugs and pain/inflammation), was up modestly in another three (diabetes, attention disorders and depression). At the same time, unit costs decreased in five traditional classes (high blood cholesterol, high blood pressure/heart disease, heartburn/ulcer disease, asthma and depression). This pattern generally reflects the continuing genericization of commonly used therapy classes.

HIGHLIGHTS

- The increase in spend for compounded medications in 2014 represented a staggering change from 2013, when compounded medications did not appear among the top 10 therapy classes. Compounded drugs strongly drove 2014 traditional trend; if excluded from the analysis, total traditional trend would have been only 2.3%.
- Another driver of positive trend among traditional therapy classes was diabetes. Trend was 18.0%, primarily from a 16.3% increase in drug costs. Much of the increase was due to continued brand innovation and brand inflation. Drug cost increases have been particularly significant among insulins, such as Lantus® (insulin glargine [rDNA origin] injection) and Levemir® (insulin detemir [rDNA origin] injection). Because insulins are manufactured by biological processes, true generics for them are not possible. But biosimilar formulations being developed are expected to cost between 20% and 40% less than the branded innovators.¹³ At least some of the increases in price for currently available insulins may have been a result of the upcoming patent expiration for Lantus and the uncertainty around biosimilar activity in the diabetes space.
- Utilization for medications used to treat high blood cholesterol decreased 2.9% after a 2.1% decrease in 2013. In addition to market saturation of generics for the most commonly used drugs, the decline may also be related to the ongoing impact of low-cost generic programs offered by retail pharmacies.
- Total trend for traditional asthma medications was -14.9%, driven by drops in utilization (3.2%) and unit cost (11.6%). The decrease in utilization is likely related to market movement toward specialty asthma medications such as Xolair® (omalizumab). Lower unit cost is due mainly to lasting impact from the August 2012 patent expiration of Merck's Singulair®. The generic, montelukast, captured 33.4% of the asthma market in 2014.
- In addition to a small increase in utilization compared to 2013, the 15.7% increase in unit cost resulted in a 16.0% spend increase for pain/inflammation medications. Large price increases for two commonly used drugs, generic opioid oxycodone/acetaminophen and branded Celebrex® (celecoxib), are driving unit cost trend. The cost of oxycodone/acetaminophen, which captured 7.3% of 2014 market share in the class, likely increased because of generic supply chain issues and new U.S. Food and Drug Administration (FDA) regulations limiting the amount of acetaminophen allowed in combination opioid products. Brand Celebrex increased in price prior to the launch of generic formulations in December 2014.

If compounded medications were excluded from the analysis, total traditional trend would have been just **2.3%** instead of **6.4%**.

DIABETES

Medications used to treat diabetes were the most expensive for the fourth year in a row when ranked by per-member-per-year (PMPY) spend, which was \$97.68, 18.0% higher than in 2013. Brand innovation continues in this traditional therapy class. Four new diabetes treatments – Farxiga™ (dapagliflozin), Tanzeum™ (albiglutide), Jardiance® (empagliflozin) and Invokamet™ (canagliflozin/metformin) – were approved in 2014. Less than half of the prescriptions filled for diabetes treatments were generic in 2014. Despite the influx of new, branded medications however, three of the most commonly used diabetes treatments – metformin, glipizide and glimepiride – are generic drugs with branded formulation patents that expired at least a decade ago. Despite having the highest PMPY cost, 2014 prevalence of use for diabetes medications was among the lowest for traditional therapy classes in the top 10.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

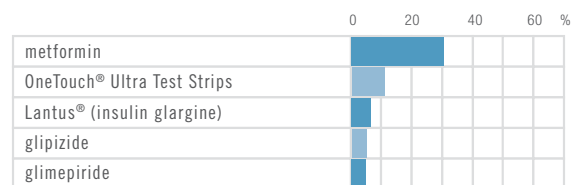
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
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3	Compounded Drugs	\$46.04	0.2%	128.2%	128.4%
4	Pain/Inflammation	\$45.98	0.3%	15.7%	16.0%
5	High Blood Pressure/Heart Disease	\$36.06	-0.4%	-12.2%	-12.6%
6	Heartburn/Ulcer Disease	\$33.40	-1.4%	-9.2%	-10.6%
7	Asthma	\$29.59	-3.2%	-11.6%	-14.9%
8	Attention Disorders	\$27.97	3.4%	2.9%	6.3%
9	Depression	\$25.98	2.1%	-20.5%	-18.4%
10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

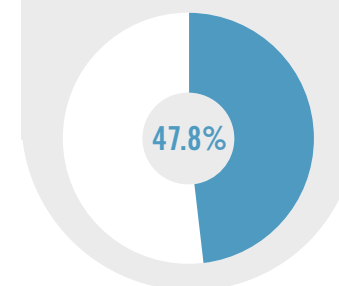
38.9% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.881 NUMBER OF PRESCRIPTIONS (PMPY)

5.1% PREVALENCE OF USE

\$110.86 AVERAGE COST PER PRESCRIPTION

HIGH BLOOD CHOLESTEROL

A 3.9% decline in unit cost and a 2.9% drop in utilization contributed to an overall 6.8% decrease in per-member-per-year (PMPY) spend for high blood cholesterol treatments in 2014. The market saturation of generic drugs continues to fuel declines in drug prices. In addition, one of the last remaining brand statins, Crestor® (rosuvastatin), is set to lose patent protection in 2016. However, a new class of biologic products known as PCSK9 inhibitors, which is in development, represents a novel way to lower cholesterol. Although initial approval of these agents likely will be to treat rare forms of hypercholesterolemia, their potential expanded use as adjunctive therapies to reduce low-density lipoproteins (LDL) for a wider population could impact drug spend significantly. This will impact specialty drug trend in the future. Atorvastatin, the active ingredient in Lipitor®, is the most commonly used medication in this class.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

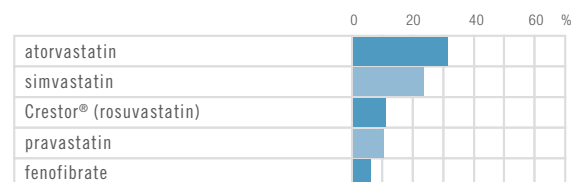
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Diabetes	\$97.68	1.7%	16.3%	18.0%
2	High Blood Cholesterol	\$48.73	-2.9%	-3.9%	-6.8%
3	Compounded Drugs	\$46.04	0.2%	128.2%	128.4%
4	Pain/Inflammation	\$45.98	0.3%	15.7%	16.0%
5	High Blood Pressure/Heart Disease	\$36.06	-0.4%	-12.2%	-12.6%
6	Heartburn/Ulcer Disease	\$33.40	-1.4%	-9.2%	-10.6%
7	Asthma	\$29.59	-3.2%	-11.6%	-14.9%
8	Attention Disorders	\$27.97	3.4%	2.9%	6.3%
9	Depression	\$25.98	2.1%	-20.5%	-18.4%
10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

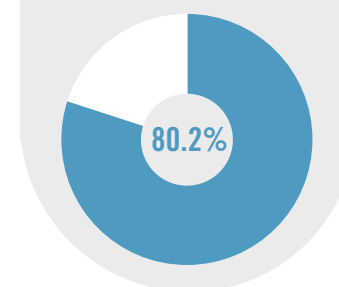
29.0% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

1.141 NUMBER OF PRESCRIPTIONS (PMPY)

11.0% PREVALENCE OF USE

\$42.69 AVERAGE COST PER PRESCRIPTION

COMPOUNDED DRUGS

Compounded drugs ranked in the top 10 therapy classes for the first time. Since the implementation of new regulations in 2012 requiring that all components of compounded drugs be specified and billed at the ingredient level rather than being rolled up under the highest priced ingredient, bulk manufacturers and compounding pharmacies have raised prices substantially for the components of many compounded drugs. The result has been unsustainable cost increases. If compounded drugs were excluded, traditional drug trend would have been only 2.3% (vs. 6.4%) and total overall trend would have been 10.4% (vs. 13.1%). Many of the compounded medications billed under the pharmacy benefit contained ingredients used to treat pain.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

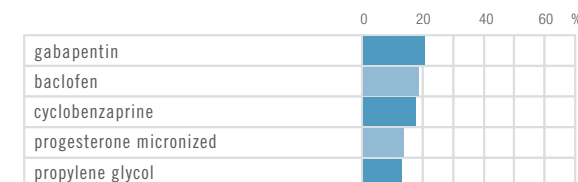
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TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

Total trend for compounded drugs – **128.4%** – was higher than trend for any other top 10 traditional therapy class.

TOP INGREDIENTS

BY VOLUME



BY THE NUMBERS

0.040 NUMBER OF PRESCRIPTIONS (PMPY)

1.4% PREVALENCE OF USE

\$1,164.12 AVERAGE COST PER PRESCRIPTION

PAIN/ INFLAMMATION

A marginal increase in utilization (0.3%) combined with a significant increase in unit cost (15.7%) contributed to a 16.0% increase in per-member-per-year (PMPY) spend for pain/inflammation medications in 2014. Although generic medications continue to dominate the class, PMPY spend has not declined in accordance. This is because manufacturers of newer versions of branded, tamper-resistant formulations have been successful in blocking generic market saturation with claims of superior safety. Together, the five most commonly used drugs, all generics, captured 55.1% of market share.

A study showed that **78.5%** of patients prescribed pregabalin treatment for neuropathic pain discontinued therapy within one year.¹⁴

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

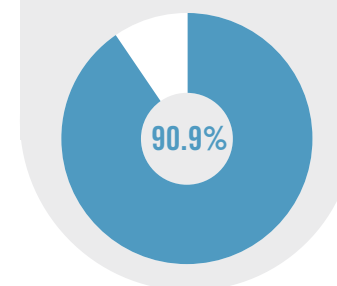
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TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

TOP DRUGS

BY MARKET SHARE

	0	20	40	60	%
hydrocodone/acetaminophen					20
gabapentin					10
tramadol					10
meloxicam					10
oxycodone/acetaminophen					10

GENERIC FILL RATE (GFR)



BY THE NUMBERS

1.127 NUMBER OF PRESCRIPTIONS
(PMPY)

22.7% PREVALENCE
OF USE

\$40.82 AVERAGE COST
PER PRESCRIPTION

HIGH BLOOD PRESSURE/HEART DISEASE

Per-member-per-year (PMPY) spend for medications used to treat high blood pressure/heart disease decreased 12.6%, to \$36.06, driven by a 12.2% decrease in unit cost. Generic medications made up 93.5% of total 2014 market share, in part due to the final approval and subsequent launch of generics to brand Diovan® (valsartan), which legal issues had delayed more than a year. The number of PMPY prescriptions for high blood pressure/heart disease medications was the highest among the traditional therapy classes in the top 10.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

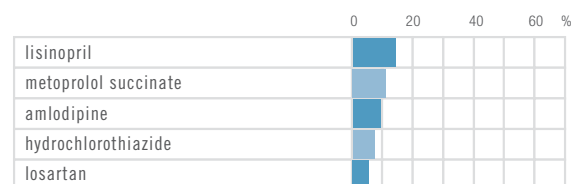
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
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TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

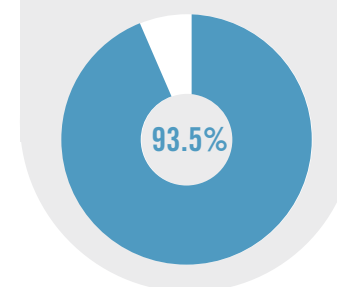
31.6% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

2.493 NUMBER OF PRESCRIPTIONS (PMPY)

16.9% PREVALENCE OF USE

\$14.46 AVERAGE COST PER PRESCRIPTION

HEARTBURN/ ULCER DISEASE

Per-member-per-year (PMPY) spend for medications used to treat heartburn and ulcer diseases such as gastroesophageal reflux disease (GERD) decreased 10.6%, to \$33.40, fueled by a 9.2% decrease in unit cost and a 1.4% decline in utilization. The decline in utilization is due primarily to a shift to the over-the-counter (OTC) version of Nexium® (esomeprazole magnesium), which became available in May 2014. With generic medications now making up 77.0% of total market share in the class, it is not surprising that the average cost per prescription dropped from \$62.08 in 2013 to \$56.26 in 2014.

A recent review of studies examining the utilization of proton pump inhibitors (PPIs) suggests that adherence among patients using PPI ranges between **53.8%** and **67.7%**.¹⁵

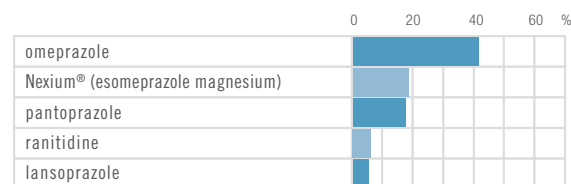
COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

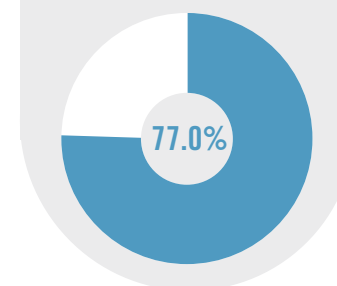
RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
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9	Depression	\$25.98	2.1%	-20.5%	-18.4%
10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.594 NUMBER OF PRESCRIPTIONS (PMPY)

8.3% PREVALENCE OF USE

\$56.26 AVERAGE COST PER PRESCRIPTION

ASTHMA

Although the generic fill rate (GFR) for asthma medications was the lowest of any top 10 traditional therapy class, per-member-per-year (PMPY) spend for asthma medications dropped 14.9% in 2014, to \$29.59, due primarily to an 11.6% decrease in unit cost. Asthma also dropped in rank from the fifth to the seventh most expensive therapy class from 2013 to 2014. Montelukast, the generic formulation of Singulair®, continued to capture more market share than any other medication. Asthma medications had a relatively high average cost per prescription in 2014, although two of the five most commonly used drugs in the class were generics.

54.9% of adult patients and
78.3% of pediatric patients are
nonadherent to medication therapy.

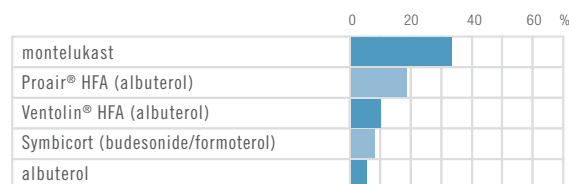
COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

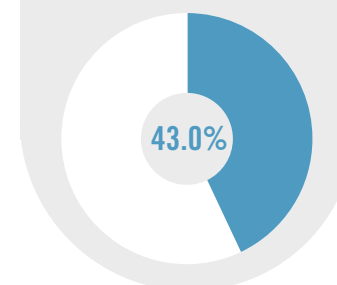
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			UTILIZATION	UNIT COST	TOTAL
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10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.431 NUMBER OF PRESCRIPTIONS
(PMPY)

8.8% PREVALENCE
OF USE

\$68.60 AVERAGE COST
PER PRESCRIPTION

ATTENTION DISORDERS

Per-member-per-year (PMPY) spend for medications used to treat attention disorders increased 6.3% in 2014, driven by a 3.4% increase in utilization and a 2.9% increase in unit cost. A non-controlled drug, Intuniv™ (guanfacine), first approved in 1986 as the blood pressure medication Tenex®, was reapproved in September 2009 as an extended-release product for attention deficit hyperactive disorder (ADHD). The first generic for Intuniv entered the U.S. market in December 2014, and others are expected to launch in mid-2015.

Recent research suggests that medication adherence may be less than **12%** in adult ADHD patients taking stimulant medications such as methylphenidate.¹⁶

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

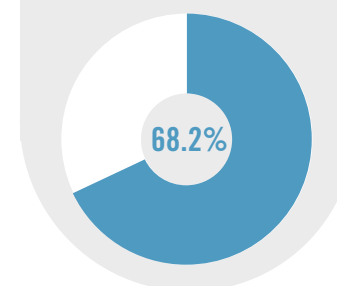
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10	Mental/Neurological Disorders	\$24.85	-0.5%	9.6%	9.1%
TOTAL TRADITIONAL		\$668.75	-0.1%	6.5%	6.4%

TOP DRUGS

BY MARKET SHARE

	0	20	40	60	%
amphetamine/dextroamphetamine					40%
methylphenidate					20%
Vyvanse® (lisdexamfetamine)					15%
Strattera® (atomoxetine)					5%
Intuniv™ (guanfacine)					2%

GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.222 NUMBER OF PRESCRIPTIONS (PMPY)

2.6% PREVALENCE OF USE

\$126.11 AVERAGE COST PER PRESCRIPTION

DEPRESSION

Utilization of medications used to treat depression increased 2.1%, but a 20.5% decrease in unit cost contributed significantly to negative overall trend. Recent literature has noted rising use of antidepressants due to increases in both the prevalence of depression and the duration of therapy for the condition.¹⁷ In 2014 alone, the generic fill rate (GFR) for the depression therapy class climbed from 88.4% to 95.9%, and only one brand drug, Viibryd® (vilazodone), remains among the top 10 most commonly used medications in this class.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

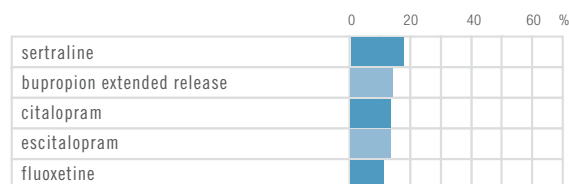
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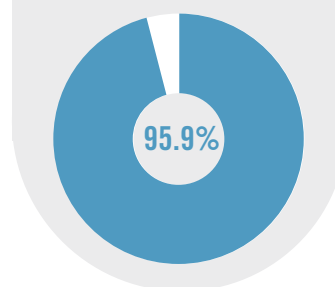
40.2% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.905 NUMBER OF PRESCRIPTIONS (PMPY)

10.0% PREVALENCE OF USE

\$28.72 AVERAGE COST PER PRESCRIPTION

MENTAL/ NEUROLOGICAL DISORDERS

A significant increase in unit cost (9.6%) contributed to the 9.1% increase in per-member-per-year (PMPY) spend for mental/neurological disorders treatments in 2014. An antipsychotic, Abilify® (aripiprazole), which captured 16.3% of market share in 2014, faces the impending loss of patent protection in April 2015 and experienced a significant increase in unit cost. Price increases often are seen in the months before a brand drug's patent expires.

COMPONENTS OF TREND FOR THE TOP 10 TRADITIONAL THERAPY CLASSES

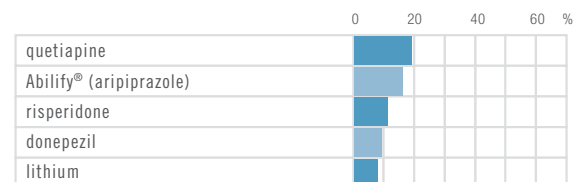
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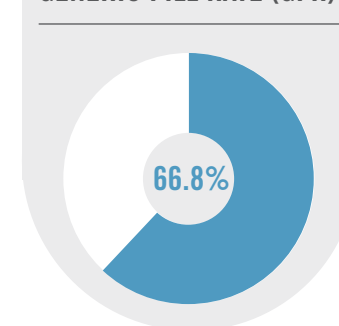
42.1% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



GENERIC FILL RATE (GFR)



BY THE NUMBERS

0.118 NUMBER OF PRESCRIPTIONS (PMPY)

1.5% PREVALENCE OF USE

\$209.96 AVERAGE COST PER PRESCRIPTION

TOP 10 TRADITIONAL DRUGS

Nine of the top 10 drugs when ranked by PMPY spend in 2014 were branded medications, accounting for 18.4% of total traditional spend. The lone generic, duloxetine, the active ingredient in Cymbalta®, climbed to sixth place in its first full year of availability. Cymbalta's patent expired in December 2013 and duloxetine's total trend was 2,010.7%, reflecting the ongoing utilization switch from the branded formulation of Cymbalta to the generic formulation throughout 2014 (the generic was only available for a short time in 2013). Nexium again had the highest PMPY spend at \$24.02, followed by Crestor at \$17.89. Among the top 10, utilization trend was marginally or significantly negative for seven drugs, but all except duloxetine showed at least a 3.9% increase in unit cost, with the highest for Humalog, at 36.1%.

Although total trend for Nexium was **-5.7%**, it remained as the most expensive traditional drug therapy used by commercially insured beneficiaries.

TOP 10 TRADITIONAL THERAPY DRUGS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL TRADITIONAL SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Nexium® (esomeprazole magnesium)	Ulcer Disease	\$24.02	3.6%	-16.5%	10.8%	-5.7%
2	Crestor® (rosuvastatin)	High Blood Pressure/Heart Disease	\$17.89	2.7%	-6.2%	10.4%	4.2%
3	Lantus® (insulin glargine)	Diabetes	\$17.55	2.6%	0.5%	34.0%	34.4%
4	Abilify® (aripiprazole)	Mental/Neurological Disorders	\$14.65	2.2%	-0.2%	16.9%	16.8%
5	Humalog® (insulin lispro)	Diabetes	\$13.87	2.1%	57.1%	36.1%	93.2%
6	duloxetine	Depression	\$11.36	1.7%	2,622.6%	-611.9%	2,010.7%
7	OneTouch Ultra® Test Strips	Diabetes	\$9.40	1.4%	-4.1%	3.9%	-0.1%
8	AndroGel® (testosterone gel)	Hormonal Supplementation	\$9.10	1.4%	-21.3%	12.4%	-9.0%
9	Lialda® (mesalamine)	Inflammatory Conditions	\$8.48	1.3%	-1.4%	11.8%	10.4%
10	Januvia® (sitagliptin)	Diabetes	\$8.15	1.2%	-0.7%	16.6%	15.9%

COMMERCIALLY INSURED: SPECIALTY THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Inflammatory Conditions	\$80.03	8.5%	15.7%	24.3%
2	Multiple Sclerosis	\$52.36	3.2%	9.7%	12.9%
3	Oncology	\$41.64	8.9%	11.7%	20.7%
4	Hepatitis C	\$37.95	76.1%	666.6%	742.6%
5	HIV	\$27.24	4.5%	10.3%	14.8%
6	Miscellaneous Specialty Conditions	\$11.10	27.3%	8.2%	35.6%
7	Growth Deficiency	\$9.98	-0.9%	7.5%	6.6%
8	Hemophilia	\$5.49	-0.8%	17.6%	16.9%
9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

Per-member-per-year (PMPY) spend for the top three specialty therapy classes – inflammatory conditions, multiple sclerosis and oncology – contributed 55.9% of the spend for all specialty medications billed through the pharmacy benefit in 2014. Drugs for inflammatory conditions (such as rheumatoid arthritis and psoriasis) continued to hold the top spot. The class of drugs used to treat hepatitis C was not even among the top 10 specialty classes in 2013. However, just three hepatitis C medications – Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir) made up 96.4% of total hepatitis C spend and 11.8% of total specialty spend, propelling the class to the fourth most expensive specialty therapy class. In 2014, decreased spend for specialty anticoagulant medications, combined with significant growth in unit cost for drugs that treat and prevent hemophilia episodes, led to the displacement of specialty anticoagulants

from the top 10. For the first time, drugs used for primary prevention and treatment of acute bleeding in hemophilia patients were among the most expensive specialty classes ranked by PMPY spend.

The class of drugs used to treat hepatitis C was not even among the top 10 specialty classes in 2013. However, just three hepatitis C medications – Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir) – made up 96.4% of total Hepatitis C spend and 11.8% of total specialty spend.

HIGHLIGHTS

- Increases in both utilization and unit cost of oncology medications contributed to a 20.7% increase in PMPY spend for the therapy class. With new, highly targeted therapies increasingly being approved, oncology drugs continue to rank among the most expensive therapies; but growth in spending is tempered by the fact that many of the new drugs are indicated for rare types of cancer. The utilization increase likely is related to advances in cancer survivorship – more patients are living longer with some types of the disease, which now often can be treated like chronic illnesses that require ongoing therapy.
- The 35.6% increase in total spend for medications used to treat miscellaneous specialty conditions – many of which are orphan conditions, including narcolepsy, nephropathic cystinosis and chorea associated with Huntington disease – is attributable primarily to increases in the costs of individual drugs. Drug costs continue to rise as manufacturers provide products to captive patient populations with few other options.
- Trend for hemophilia medications was 16.9% in 2014, driven by a double-digit increase in unit costs. Two-thirds of market share in this class is captured by formulations of desmopressin, a generic medication frequently used for milder cases. Brand inflation occurred for clotting factors such as BeneFix® (coagulation factor IX [recombinant]) and Feiba NF (anti-inhibitor coagulation complex), helping drive an increase in unit cost.
- Spend for transplant-rejection medications continued to decline in 2014, dropping 2.3% due in large part to the increasing availability of lower-cost generic formulations. In January 2014, two of the few remaining brand immunosuppressant drugs for post-transplant use, Myfortic® (mycophenolic acid) and Rapamune® 0.5mg tablets (sirolimus), lost patent protection, contributing significantly to the 86.1% generic fill rate (GFR) in this therapy class.

Specialty medications accounted for more than **31%** of total drug spend in 2014, up from **27.7%** in 2013.

INFLAMMATORY CONDITIONS

Inflammatory conditions was the most expensive specialty therapy class for the sixth year in a row, resulting from an 8.5% increase in utilization and a 15.7% increase in unit cost. The greater utilization is due to the prevalence of rheumatoid arthritis (RA), the most common condition these medications treat, and an expansion in approved indications for some of the most commonly used drugs in the class. The 15.7% increase in unit cost is likely related to typical brand inflation. Two drugs with multiple indications, Humira® (adalimumab) and Enbrel® (etanercept), continued to account for more than 80% of market share. Doubling its market share from 2013 to 2014 was Xeljanz® (tofacitinib), the only oral disease modifying anti-rheumatic drug indicated to treat RA that has not responded to other therapies. At the time of approval by the FDA in 2012, questions concerning its safety profile made its place in therapy unclear. As longer-term safety and effectiveness data have become available, however, prescribers and patients are more accepting of using Xeljanz.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

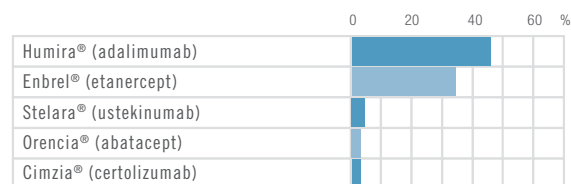
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Inflammatory Conditions	\$80.03	8.5%	15.7%	24.3%
2	Multiple Sclerosis	\$52.36	3.2%	9.7%	12.9%
3	Oncology	\$41.64	8.9%	11.7%	20.7%
4	Hepatitis C	\$37.95	76.1%	666.6%	742.6%
5	HIV	\$27.24	4.5%	10.3%	14.8%
6	Miscellaneous Specialty Conditions	\$11.10	27.3%	8.2%	35.6%
7	Growth Deficiency	\$9.98	-0.9%	7.5%	6.6%
8	Hemophilia	\$5.49	-0.8%	17.6%	16.9%
9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

39.6% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.027 NUMBER OF PRESCRIPTIONS (PMPY)

0.3% PREVALENCE OF USE

\$2,913.33 AVERAGE COST PER PRESCRIPTION

MULTIPLE SCLEROSIS

A 9.7% increase in unit cost was the key driver of the 12.9% increase in per-member-per-year (PMPY) spend for multiple sclerosis (MS) medications. New oral medications continue to change the treatment landscape in this therapy class. Together, Tecfidera® (dimethyl fumarate, approved in 2013) and Gilenya® (fingolimod, approved in 2010) captured 29.8% of market share in 2014. The new longer-acting formulation of Copaxone® (glatiramer) was the class leader with 29.7% of market share. A new interferon product, Plegridy™ (peginterferon beta-1a), received approval by the FDA in August 2014 as a longer-lasting treatment for MS, but it has not impacted trend yet. Recommended dosing for Plegridy is once every two weeks by subcutaneous injection, rather than the weekly intramuscular dosing for Avonex® (interferon beta-1a). The average cost per prescription in this class increased 9.2% to \$4,510.06 in 2014.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

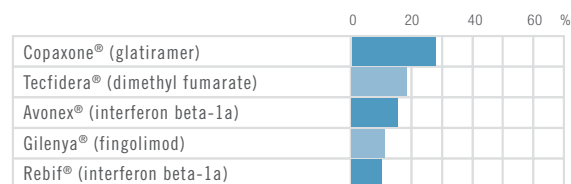
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10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

23.0% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.012 NUMBER OF PRESCRIPTIONS (PMPY)

0.1% PREVALENCE OF USE

\$4,510.06 AVERAGE COST PER PRESCRIPTION

ONCOLOGY

Per-member-per-year (PMPY) spend for oncology medications was \$41.64 in 2014. Although the increase in spend for this class of medications has slowed in comparison to the PMPY trend observed in previous years, trend was still 20.7% in 2014, spurred by an 8.9% increase in utilization and an 11.7% increase in unit cost. Unit cost increases for Gleevec® (imatinib), which captured 12.5% of market share, and Revlimid® (lenalidomide), which captured 10.8% of market share, were prime contributors. Temozolomide, a generic for Temodar® that launched in 2013, continued to capture market share. In addition, generics to Xeloda® (capecitabine) that were launched in 2014 were the fourth most commonly used oncology medications for the year. However, nine new branded oncology therapies that were approved for use in 2014 are likely to have an impact on the class going forward.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

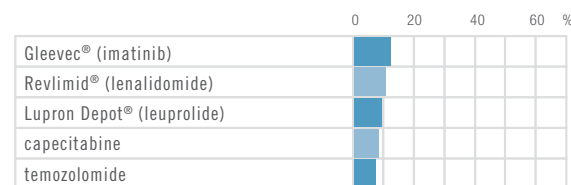
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10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

38.2% of patients are nonadherent to medication therapy (oral oncology).

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.007 NUMBER OF PRESCRIPTIONS (PMPY)

0.1% PREVALENCE OF USE

\$6,191.29 AVERAGE COST PER PRESCRIPTION

HEPATITIS C

Per-member-per-year (PMPY) spend for hepatitis C medications increased 742.6% to \$37.95 in 2014, propelling this class of drugs to the fourth most expensive specialty therapy class when ranked by PMPY spend. Hepatitis C medications did not rank in the top 10 list in 2013. These changes were driven entirely by newly approved clinical breakthroughs for the treatment of hepatitis C. Sovaldi® (sofosbuvir) and Olysio® (simeprevir) that were approved in 2013 along with Harvoni® (ledipasvir/sofosbuvir), approved in October 2014, jumped into the top five for the class. This new generation of oral antiviral medications offers clinical benefits that are superior to earlier therapies. Their price tags, however, are unsustainable. At approximately \$84,000 for one 12-week course of treatment, Sovaldi alone captured 37.5% of the 2014 market share for hepatitis C.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

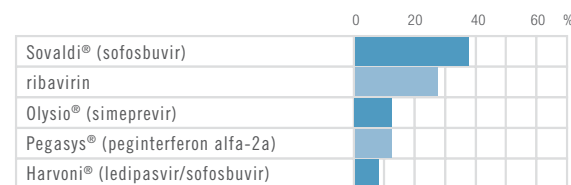
RANKED BY 2014 PMPY SPEND

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9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

11.7% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.002 NUMBER OF PRESCRIPTIONS (PMPY)

0.03% PREVALENCE OF USE

\$16,373.40 AVERAGE COST PER PRESCRIPTION

HIV

Per-member-per-year (PMPY) spend for HIV medications increased 14.8% from 2013 to 2014, primarily due to a 10.3% increase in unit cost. The average cost per prescription for more than two-thirds of the HIV medications on the market in 2014 exceeded \$1,000 per prescription, compared with slightly more than half of the HIV medications on the market in 2013. The 10 most commonly used medications were all branded drugs; the top two were combination therapies that each contain more than one active ingredient in a single pill.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

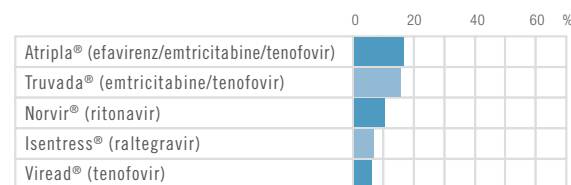
RANKED BY 2014 PMPY SPEND

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			UTILIZATION	UNIT COST	TOTAL
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9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

23.0% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.024 NUMBER OF PRESCRIPTIONS (PMPY)

0.14% PREVALENCE OF USE

\$1,138.48 AVERAGE COST PER PRESCRIPTION

MISCELLANEOUS SPECIALTY CONDITIONS

The class of medications used to treat an assortment of specialty conditions, many of them orphan diseases, is ranked sixth in the top 10 most expensive specialty therapy class for 2014. The class includes Xenazine® (tetrabenazine), used to treat Huntington's disease; Xyrem® (sodium oxybate), used to treat narcolepsy; and Arestin® (minocycline), used to treat periodontal disease. Many medications in this class are only available through a limited network of specialty pharmacies. Several medications in this therapy class also have substantial average costs per prescription, but a 27.3% increase in utilization in 2014 mainly drove the 35.6% total trend – the second highest of the specialty therapy classes in the top 10. The five most commonly used medications captured 83.2% of the market share in this therapy class.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

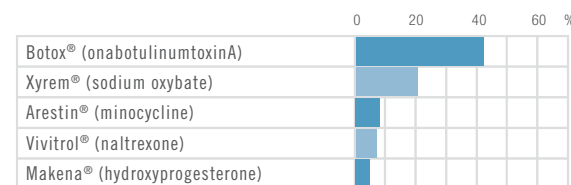
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Inflammatory Conditions	\$80.03	8.5%	15.7%	24.3%
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9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

Nearly **40%** of the drugs in this therapy class have been approved as orphan drugs.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.002 NUMBER OF PRESCRIPTIONS (PMPY)

0.06% PREVALENCE OF USE

\$4,539.50 AVERAGE COST PER PRESCRIPTION

GROWTH DEFICIENCY

The utilization of medications indicated to treat growth deficiency decreased by almost 1% in 2014, but a 7.5% increase in unit cost resulted in a 6.6% increase in per-member-per-year (PMPY) spend. Norditropin® FlexPro® (somatropin), whose market share continues to grow year-over-year, was the most commonly used medication in this class in 2014. The top two drugs in this class accounted for more than two-thirds of market share. The overall prevalence of human growth hormone use, however, remained extremely low. Less than 0.05% of commercially insured beneficiaries filled a prescription for one of these medications in 2014.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

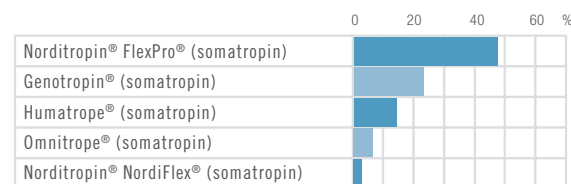
RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
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9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

37.7% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.003 NUMBER OF PRESCRIPTIONS (PMPY)

0.03% PREVALENCE OF USE

\$3,852.58 AVERAGE COST PER PRESCRIPTION

HEMOPHILIA

The steady increase in spend for hemophilia drugs brought the class into the top 10 most-expensive specialty therapy classes when ranked by per-member-per-year (PMPY) spend. With a 16.9% trend, spend for hemophilia is increasing at a faster rate than that for drugs used to treat much more common conditions, such as multiple sclerosis and HIV. Trend was driven by a 17.6% increase in unit costs. Desmopressin captured two-thirds of the market share in this class.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

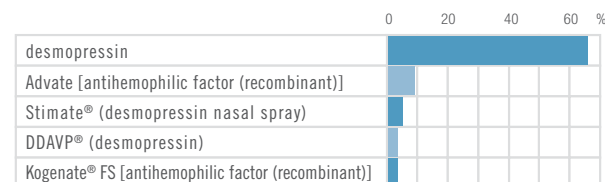
RANKED BY 2014 PMPY SPEND

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			UTILIZATION	UNIT COST	TOTAL
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2	Multiple Sclerosis	\$52.36	3.2%	9.7%	12.9%
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10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

A review of studies of hemophilia patients using prophylactic therapy suggests that **age and the presence of symptoms** were significantly related to medication adherence.¹⁸

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.001 NUMBER OF PRESCRIPTIONS (PMPY)

0.01% PREVALENCE OF USE

\$7,519.16 AVERAGE COST PER PRESCRIPTION

PULMONARY ARTERIAL HYPERTENSION

Following a relatively flat trend in 2013, spend for pulmonary arterial hypertension treatments increased 13.8% in 2014, with increases in utilization and cost contributing equally. Much of the increased utilization for the class is related to the 2012 patent expiration for Revatio® (sildenafil).

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

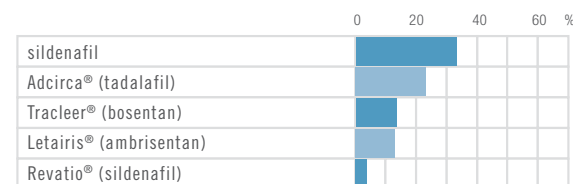
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9	Pulmonary Arterial Hypertension	\$5.41	7.6%	6.2%	13.8%
10	Transplant	\$5.13	0.8%	-3.1%	-2.3%
TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

28.3% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.001 NUMBER OF PRESCRIPTIONS (PMPY)

0.01% PREVALENCE OF USE

\$4,023.23 AVERAGE COST PER PRESCRIPTION

TRANSPLANT

Per-member-per-year (PMPY) spend for medications used to prevent organ-transplant rejection decreased 2.3% between 2013 and 2014. The unit cost trend was the primary reason, stemming from market saturation of generic drugs in the class. Generic medications captured more than 85% of total market share in 2014. Accordingly, the average cost per prescription for transplant medications was lower than that of any other specialty therapy class. A new extended-release formulation of tacrolimus, Astagraf XL® (tacrolimus extended release), was approved in July 2013 for use in kidney transplant patients, but it had little impact in the class. Generics to Rapamune® 0.5mg tablets (sirolimus) and Myfortic® (mycophenolic acid delayed-release tablets) were also launched in 2014.

COMPONENTS OF TREND FOR THE TOP 10 SPECIALTY THERAPY CLASSES

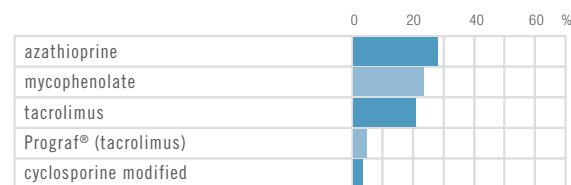
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TOTAL SPECIALTY		\$311.11	5.8%	25.2%	30.9%

33.0% of patients are nonadherent to medication therapy.

TOP DRUGS

BY MARKET SHARE



BY THE NUMBERS

0.025 NUMBER OF PRESCRIPTIONS (PMPY)

0.2% PREVALENCE OF USE

\$208.00 AVERAGE COST PER PRESCRIPTION

TOP 10 SPECIALTY DRUGS

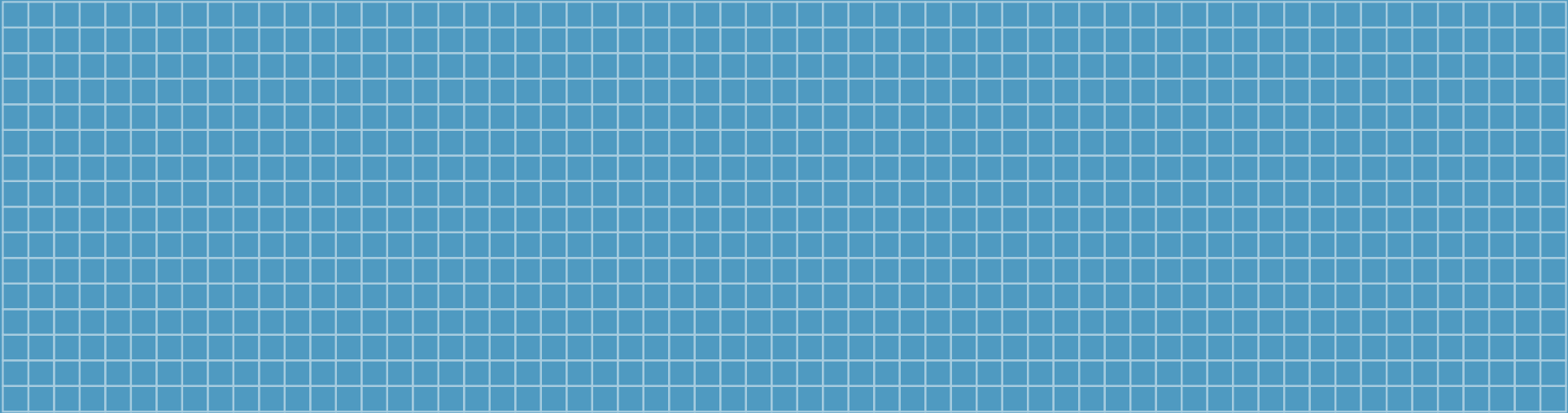
Despite a decrease in utilization for half of the drugs in the top 10 when ranked by per-member-per-year (PMPY) spend, the unit cost for all top-10 drugs increased at least 6%. Two of the new hepatitis C drugs ranked in the top 10 most-expensive drugs, even though each had been on the market for only a little over a year. Sovaldi and Olysio had the largest increases in utilization, unit cost and total trend. Part of the magnitude of increase is related to these two drugs having only been available for a single month in 2013. In these two cases, just one month's utilization in 2013 was compared to 12 months' worth of utilization in 2014. Sovaldi treats far fewer patients than the most-expensive and second-most-expensive specialty drugs when ranked by PMPY spend, Humira and Enbrel, which also ranked among the costliest specialty medications. Olysio ranked 10th. Three drugs used to treat multiple sclerosis (MS) were also among the most-expensive single therapies in 2014, ranked by PMPY spend. Tecfidera, an oral MS treatment, had a total trend of 152.1%, driven by a triple-digit increase in utilization. Two oncology drugs and one drug for HIV rounded out the most-expensive specialty drugs for 2014.

Tecfidera, an oral MS treatment, had a total trend of **152.1%**, driven by a triple-digit increase in utilization.

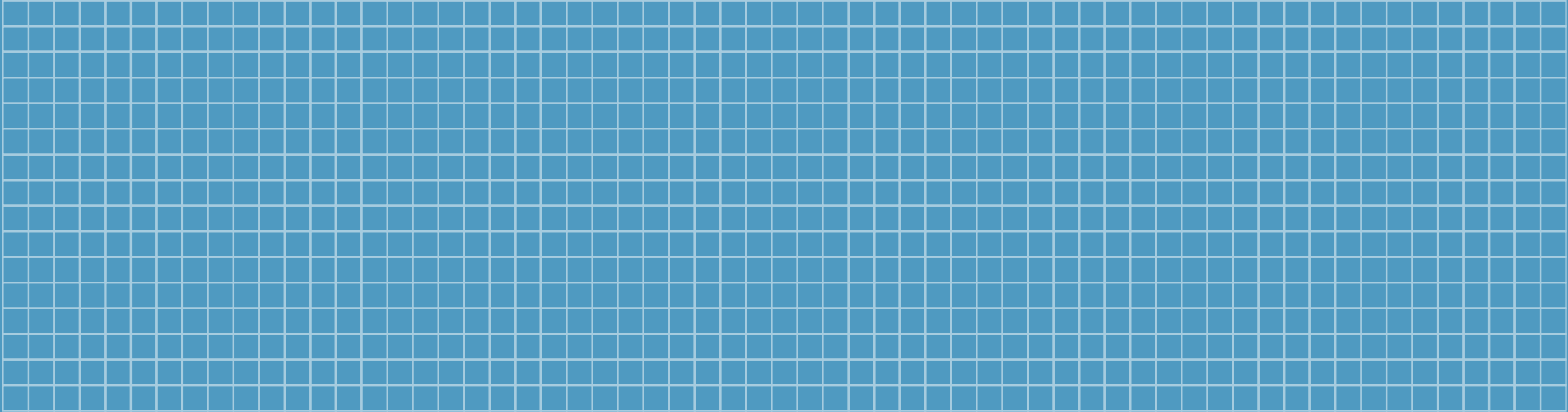
TOP 10 SPECIALTY THERAPY DRUGS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL SPECIALTY SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Humira® (adalimumab)	Inflammatory Conditions	\$37.06	11.9%	10.7%	17.1%	27.8%
2	Enbrel® (etanercept)	Inflammatory Conditions	\$25.65	8.2%	-2.2%	13.7%	11.5%
3	Sovaldi® (sofosbuvir)	Hepatitis C	\$24.38	7.8%	9,743.5%	258.4%	10,001.9%
4	Copaxone® (glatiramer)	Multiple Sclerosis	\$15.48	5.0%	-7.3%	7.2%	-0.1%
5	Tecfidera® (dimethyl fumarate)	Multiple Sclerosis	\$10.60	3.4%	130.0%	22.1%	152.1%
6	Avonex® (interferon beta-1a)	Multiple Sclerosis	\$8.18	2.6%	-17.4%	9.4%	-7.9%
7	Atripla® (efavirenz/emtricitabine/tenofovir)	HIV	\$7.42	2.4%	-4.7%	7.3%	2.6%
8	Gleevec® (imatinib)	Oncology	\$6.86	2.2%	-5.3%	17.6%	12.3%
9	Revlimid® (lenalidomide)	Oncology	\$6.85	2.2%	5.6%	6.1%	11.7%
10	Olysio® (simeprevir)	Hepatitis C	\$6.49	2.1%	14,666.0%	757.5%	15,423.6%



2015-2017 TREND FORECAST



SPEND FOR TRADITIONAL DRUGS IN THE NEXT THREE YEARS

In 2014, the trend for traditional drugs was 6.4%, with per-member-per-year (PMPY) spend at \$668.75. We anticipate that traditional trend will decline modestly in 2015 and then increase moderately in both 2016 and 2017. The significant increase in spend for traditional drugs in 2014 was driven by an unprecedented explosion in spend for compounded medications. The utilization of traditional medications is likely to increase, but the continuing decline in overall costs related to an abundance of generics and a relative lack of brand innovators in the pipeline for the most commonly used therapy classes (aside from diabetes) will keep traditional drug spend from increasing substantially. In fact, trend for five of the top therapy classes – high blood cholesterol, compounded medications, high blood pressure/heart disease, heartburn/ulcer disease and depression – is expected to be negative in 2015. The class of mental/neurological disorders will have a negative total trend in 2016 and 2017. The largest increases in the next three years are expected for only two classes – diabetes, which will continue to experience a slight increase in utilization along with escalating brand inflation, and anticoagulants, which will continue to capture market share from specialty anticoagulants such as enoxaparin and fondaparinux.

DIABETES

PMPY drug spend for diabetes medications is expected to increase 18.3% in each of the next three years. Although only slight year-over-year increases in utilization are projected, substantial continued increases in unit cost are likely to come from brand innovation, steady inflation for branded drugs and switches from older generic monotherapies to newer combination products. In addition, new, longer-acting dipeptidyl peptidase-4 (DPP-4) and human glucagon-like peptide (GLP-1) formulations are in the development pipeline. Although they will carry lower risks of causing hypoglycemia at night, they may be priced higher than similar drugs that are currently available. Finally, biosimilars to some types of insulin also are likely to enter the market in the near future, but the impact will not be felt immediately because physicians may be reluctant to change insulins for patients whose diabetes is under control. No significant patent expirations are expected in the next few years.

2015-2017 TREND FORECAST

	2015	2016	2017
TOTAL OVERALL	6.8%	10.6%	11.2%

TOP TRADITIONAL THERAPY CLASSES

2015 - 2017

THERAPY CLASS	TREND		
	2015	2016	2017
Diabetes	18.3%	18.3%	18.3%
High Blood Cholesterol	-8.5%	-14.3%	-24.7%
Compounded Medications	-45.0%	8.0%	8.0%
Pain/Inflammation	13.1%	9.4%	9.5%
High Blood Pressure/Heart Disease	-3.5%	-6.7%	-10.6%
Heartburn/Ulcer Disease	-31.4%	-34.0%	-30.7%
Asthma	12.7%	9.8%	9.9%
Attention Disorders	11.8%	11.0%	10.2%
Depression	-26.3%	-10.8%	-0.8%
Mental/Neurological Disorders	0.7%	-6.0%	-5.5%
Contraceptives	15.0%	11.0%	9.0%
Anticoagulants	25.1%	15.5%	12.3%
Other Traditional Classes	1.7%	3.1%	2.4%
TOTAL TRADITIONAL	-0.5%	3.9%	4.3%

HIGH BLOOD CHOLESTEROL

Per-member-per-year (PMPY) spend for the class is forecast to decline for the next several years as a result of decreases in both drug costs and utilization. The January 2016 expiration of the patent for Crestor® (rosuvastatin) is likely to drive down PMPY spend in 2016. Patent expirations for Zetia® (ezetimibe) and Vytorin® (ezetimibe/simvastatin) in 2017 are expected to spur an even faster decline in spend. Although guidelines for the primary and secondary prevention of atherosclerotic cardiovascular disease and events, published in late 2013, call for treatment based on risk factors rather than for the achievement of specific cholesterol levels, significant changes in prescribing patterns have yet to be seen. Although expensive new treatments known as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors that are in the development pipeline may be an alternative to statins, they will be considered specialty medications. Therefore, they will not have a significant direct impact on traditional spend for high blood cholesterol therapies. A focus on cost when PCSK9 inhibitors are introduced, however, may lead to an increase in the utilization of traditional cholesterol-lowering drugs among patients who are not currently being treated. However, any increases in utilization as a result will not offset the steep drops in drug costs for existing traditional high blood cholesterol treatments.

COMPOUNDED MEDICATIONS

Spend for compounded medications is expected to decline sharply in 2015, and then to increase again to a much more sustainable rate of 8% growth in both 2016 and 2017. Clients that implemented the compound-utilization management solution in 2014 were able to substantially control the continuing increase in cost. However, only about 60% of clients implemented the program by the end of 2014. The negative trend in 2015 is expected because clients that implemented the program in 2014 will realize more than a full-year reduction in spend by the end of 2015, and additional clients are expected to implement the program by the end of the year. The drop in spend is likely to be driven exclusively by a drop in utilization, as there is no expectation that the price increases seen for compounded medications will abate. The utilization-management program is expected to have maximum impact before 2016 and 2017, when PMPY drug spend is expected to increase moderately, primarily as a result of drug inflation.

PAIN/INFLAMMATION

For medications used to treat pain and inflammation, PMPY spend is forecast to rise moderately in each of the next several years, driven almost entirely by an increase in unit cost. Short-term use of opioids has shown a steady pattern of decline over the past five years. The Drug Enforcement Administration (DEA) reclassification of all hydrocodone combination products to schedule II controlled substances in October 2014 also may contribute to lower utilization. Drops in utilization are attenuated by the influx of branded, tamper-resistant formulations of older medications, such as OxyContin® (oxycodone), that replace or compete with non-abuse-deterrent generically available options. In addition, shortages of oxycodone/acetaminophen products may continue to elevate generic prices. Celebrex® (celecoxib), a nonsteroidal anti-inflammatory drug, lost patent protection in 2014. Because it captured so much market share, the lower cost of generic celecoxib compared to brand Celebrex is likely to decrease spend for the class as a whole; but the drop will be offset fully by increases in prices for other drugs in this class.

The lower cost of generic celecoxib is likely to decrease spend for the class, but the drop will be offset fully by increases in prices for other drugs in the class.

HIGH BLOOD PRESSURE/HEART DISEASE

The forecast decline in PMPY spend for medications used to treat high blood pressure is expected to result from stagnant utilization and the release of more generics in the class. Generics to Diovan® (valsartan), which lost patent protection in 2012, were delayed for nearly two years due to legal issues. The release of the first Diovan generic in June 2014, followed by several others in December, is expected to have a continuing impact on spend throughout 2015. Four of the remaining brand drugs – Azor® (amlodipine/olmesartan), Benicar® (olmesartan), Benicar HCT® (olmesartan/hydrochlorothiazide) – and Tribenzor® (amlodipine/olmesartan/hydrochlorothiazide) are set to lose patent protection late in 2016. The resulting decline in spend is likely to be small, however, because together they account

for less than one percent of market share. A new drug containing the angiotensin receptor blocker valsartan and sacubitril, the first in a new class called neprilysin inhibitors, could be submitted to the FDA for approval in 2015. Currently known as LCZ696, the drug may have blockbuster potential and larger-than-expected adoption of it could impact trend considerably.

HEARTBURN/ULCER DISEASE

The large year-over-year negative trend forecast for medications used to treat heartburn/ulcer disease is driven primarily by many less-expensive generic and over-the-counter (OTC) versions of the most commonly used medications in the class. Continuing decreases in PMPY spend from 2015 through 2017 are expected after the May 2014 launch of Nexium® 24HR – an OTC version of the last remaining blockbuster drug in the class, Nexium® (esomeprazole magnesium) – began to erode prescription market share. Decreasing utilization of prescription medications as patients shift to OTC Nexium will have a significant impact on trend in 2015, followed by even larger impacts in 2016 and 2017. Generic Nexium, delayed by regulatory issues for eight months, finally reached the market in early 2015. No new drugs for heartburn/ulcer disease are in development and the few remaining brands, such as Dexilant (dexlansoprazole), will have difficulty competing with the many popular generic and OTC options.

ASTHMA

PMPY spend for asthma medications is expected to increase again after the cost lowering impact of the 2012 patent expiration for Singulair® (montelukast) abates in 2015. Brand inflation among inhalers will push up cost, while increased diagnosis and subsequent initiation of treatment for asthma and chronic obstructive pulmonary disease (COPD) will combine to raise PMPY spend. In addition, increased utilization is expected as new indications for existing therapies, such as Spiriva® Respimat® (tiotropium), expand use among additional populations who were not previously using medications.

ATTENTION DISORDERS

PMPY spend for medications used to treat attention disorders is forecast to increase in each of the next three years. Utilization will increase for adults diagnosed with attention disorders and adults seeking improved ability to focus and concentrate, and utilization will continue for children and adolescents already using attention-disorder therapy. In February 2015, a new indication to treat binge-eating disorder was granted for Vyvanse® (lisdexamfetamine), one of the most commonly used drugs in the class; as a result, utilization of Vyvanse is expected to increase. However increasing generic availability is expected to slow the rate of growth in unit costs. Intuniv™ (guanfacine) went generic in late 2014, and the patent for Strattera® (atomoxetine) will expire in 2017. Still, several of the convenient, once-daily attention disorder drugs will remain under patent protection for several more years.

The utilization of traditional medications is likely to increase, but the continuing decline in overall costs related to an abundance of generics and a relative lack of brand innovators in the pipeline for the most commonly used therapy classes (aside from diabetes) will keep traditional drug spend from increasing substantially.

DEPRESSION

PMPY spend for medications used to treat depression is expected to decrease for the next several years, due mainly to slight decreases in utilization and declines in drug costs as generics become more available. The December 2013 launch of generics for one of the last remaining brand serotonin and norepinephrine reuptake inhibitors, Cymbalta® (duloxetine), will continue contributing to a significant decline in spend through 2015. But by 2016, the market will have absorbed most of the savings offered by generic medications in the class. Few new antidepressant therapies are in the pipeline, though, so in 2017 trend should essentially be flat.

MENTAL/NEUROLOGICAL DISORDERS

The forecast for medications used to treat mental/neurological disorders hinges on the introduction of generic competition to the blockbuster atypical antipsychotic, Abilify® (aripiprazole), in May 2015. Abilify captured more market share than any other drug in this class, and its price has been increasing in advance of the revenue loss to the manufacturer. The effect of generics to the Alzheimer's disease medication, Namenda® (memantine), expected in July 2015, will be tempered because the manufacturer already has switched a majority of patients to a newer once-daily formulation, Namenda XR® (memantine extended release). Because Namenda XR is patent-protected until 2029, the profits of the brand franchise will be extended despite generic competition. Still, other major generic medications – such as quetiapine and olanzapine, which will continue to account for significant market share in the class – will contribute to negative trend beginning in 2016. Utilization is expected to increase marginally from increased use of atypical antipsychotics to treat bipolar disorder and treatment-resistant depression. The new drugs in the pipeline, if approved, will have as competitors the many commonly used generic medications available within this class.

CONTRACEPTIVES

The year-over-year trend forecast for contraceptives is influenced heavily by the Patient Protection and Affordable Care Act's (ACA) mandate that patients be provided some form of contraception at zero cost to them. Surprisingly, no significant increase has been seen in utilization of contraceptive methods commonly billed through the pharmacy benefit. The increases in utilization that have occurred have been for long-acting, reversible contraceptives, typically billed through the medical benefit. Unit cost increases, which are expected as a result of the continued cost-share shift to payers, likely will taper off after 2015. Increased drug spend anticipated for 2016 and 2017 will result from brand inflation, in as much as the many generic options available in the class are likely to compete with new strengths, dosage forms and branded reformulations of older drugs.

ANTICOAGULANTS: A CLASS TO WATCH

PMPY spend for newer oral traditional anticoagulants like Xarelto® (rivaroxaban) and Eliquis® (apixaban) is expected to grow significantly in the next few years. The rise will be driven by increased utilization in the traditional anticoagulants class from 2015 forward, as patients continue to switch from less convenient injectable specialty medications like enoxaparin and fondaparinux. Costs are expected to increase significantly, however, because physicians are more likely to prescribe new patients one of the newer, brand-only oral anticoagulants rather than warfarin, which although vastly less expensive, is much less convenient. In addition, approvals of new anticoagulant reversal agents in the pipeline for the newer anticoagulants are expected to shift current users of warfarin, which can be reversed, if needed, to the newer medications.

The trend for **five** of the top therapy classes – high blood cholesterol, compounded medications, high blood pressure/heart disease, heartburn/ulcer disease and depression – is expected to be **negative** in 2015.

SPEND FOR SPECIALTY DRUGS IN THE NEXT THREE YEARS

In 2014, the trend for specialty drugs was 30.9%, with per-member-per-year (PMPY) spend at \$311.11. PMPY spend was higher than what was predicted in 2014 because of the significant impact of the new hepatitis C treatments.

Although specialty trend will slow to more sustainable levels in the next three years, it still is expected to experience fairly stable double-digit growth in 2015, 2016 and 2017 (22.6%, 22.3% and 21.3% respectively). Continuing increases in utilization are likely as indications expand for existing drugs and specialty therapies are prescribed more often. However, the major contributors to rising PMPY spend for specialty medications are brand inflation and the accelerating development of expensive, highly targeted therapies.

INFLAMMATORY CONDITIONS

The basis for the per-member-per-year (PMPY) trend forecast for medications used to treat inflammatory conditions – such as rheumatoid arthritis, psoriasis and Crohn's disease – is sustained increases in both utilization and treatment costs. The class will continue to be dominated by expensive branded, biologic medications. Utilization will increase due to the expansion of indications for current therapies, movement of therapy from medical settings to pharmacy and increasing numbers of patients newly diagnosed with inflammatory conditions. Generally, prevalence of certain autoimmune conditions is going up, but the reasons are not understood. Although some of the market share in the class may shift to new treatments that are expected to be available in 2015 and 2016, price parity with existing drugs is expected. Most current medications in this class will retain patent protection for the foreseeable future, with the exception of the scheduled Dec. 31, 2016, patent expiration for Humira® (adalimumab). Although several companies are in late stages of clinical trials for a biosimilar to Humira, it is unclear if these therapies will be able to mitigate trend growth in 2017.

TREND FORECAST FOR KEY SPECIALTY THERAPY CLASSES

2015 - 2017

THERAPY CLASS	TREND FORECAST*		
	2015	2016	2017
Inflammatory Conditions	21.6%	21.6%	21.1%
Multiple Sclerosis	11.3%	6.5%	3.0%
Oncology	21.6%	20.4%	19.8%
Hepatitis C	66.5%	55.4%	44.3%
HIV	17.3%	16.6%	16.2%
Miscellaneous Specialty Conditions	31.1%	29.7%	28.2%
Growth Deficiency	12.5%	10.4%	10.5%
Hemophilia	3.9%	3.3%	3.4%
Pulmonary Arterial Hypertension	12.5%	12.0%	12.1%
Transplant	-5.8%	-1.3%	0.0%
Hereditary Angioedema	22.5%	24.2%	20.7%
Other Specialty Classes	6.7%	6.7%	6.4%
TOTAL SPECIALTY	22.6%	22.3%	21.3%

*Trend is forecast only for specialty medications billed through the pharmacy benefit.

MULTIPLE SCLEROSIS

The biggest driver of the PMPY trend forecast for medications used to treat multiple sclerosis (MS) over the next three years is continued brand inflation, offset to some extent by generics to Copaxone® 20mg (glatiramer). Moderate inflation rates in this class will contribute to the rising costs of treating MS in the next few years. Copaxone 20mg will likely represent approximately 25% of the Copaxone market share by the time generics for it are available in September 2015. However, limited generic competition is expected at first, which may limit uptake and cost relief in the short-term after generics launch. An oral medication, Tecfidera® (dimethyl fumarate), still is capturing market share from older, injectable medications. Ponesimod, a new oral pipeline drug that might be launched in 2017, may increase spend as well.

Moderate inflation rates for multiple sclerosis (MS) drugs will contribute to the rising cost of treating the disease in the next few years.

ONCOLOGY

The year-over-year trend forecast for oncology medications is based on continuations of brand inflation and brand-drug innovation; both also will increase utilization. Increasingly, many cancers can be treated as chronic conditions, requiring longer and sometimes more complex treatment. Multiple therapies can be used sequentially or as combination treatment – leading to increased utilization. In addition, more cancer treatments are being managed through the pharmacy benefit rather than the medical benefit, which will be reflected in both spend and utilization because of improved visibility. Newer, often more-expensive oral oncology treatments continue to be approved and capture market share. Generics to Gleevec® (imatinib) are expected in 2016 and their competition will slightly mitigate trend growth; however, high prices for new and existing branded drugs will minimize the impact on trend.

HEPATITIS C

In the next three years, further significant increases in the PMPY trend for hepatitis C treatments will result from increases in utilization and brand inflation. Most individuals with hepatitis C either do not know they have the virus or have not yet been treated for it. This suggests an increase in the utilization of treatments over the next few years is likely, as newly diagnosed patients seek therapy. Although immediate treatment is not critical for newly diagnosed patients, both lowered costs for the drugs and more attention paid to this therapy class are expected to contribute to increased utilization. Also, as a result of more-affordable pricing for newer therapies, physicians are expected to increase prescribing, returning from the slowdown in prescribing which occurred in mid-2014. Still, large cost increases in 2014 were associated with the introduction of four highly effective therapies to the U.S. market. The addition of Viekira Pak™ (ombitasvir/paritaprevir/ritonavir with dasabuvir) to formularies, however, will limit near-term changes in unit cost to typical brand inflation.

Most individuals with hepatitis C either do not know they have the virus or have not yet been treated for it, suggesting an increase in the utilization of treatments over the next few years is likely as newly-diagnosed patients seek therapy.

HIV

The year-over-year trend forecast for medications used to treat HIV is based on modest utilization growth along with double-digit increases in unit cost. Because screening for HIV is more accessible and a greater percentage of patients are surviving, utilization continues to increase slightly. The greatest HIV market share is held by newer, branded medications that combine several medications into one dose, minimizing pill burden and helping increase adherence. Only limited utilization of generic HIV medications is expected because some are poorly tolerated and many are inconvenient, single-drug products that require numerous daily doses, must be taken with other drugs or have complicated dosing patterns. Although strong

brand innovation is not expected, new, single-tablet regimens without the inconveniences of many generics will continue to play an important role in this market. In addition, no abatement is expected for typical brand inflation of the already-expensive medications in the class.

MISCELLANEOUS SPECIALTY CONDITIONS

Medications used to treat less-common specialty conditions, many of them orphan diseases, are forecast to increase significantly in the next few years, driven by both brand inflation and increased utilization. Medications for miscellaneous specialty conditions include Xyrem® (sodium oxybate), which treats cataplexy and excessive daytime sleepiness in narcolepsy, and Xenazine® (tetrabenazine), which treats involuntary movements (chorea) for patients with Huntington's disease. Most drugs in the class have little or no competition for market share and patients generally have no alternative options. The pharmaceutical landscape will be brighter for patients with presently untreatable orphan conditions in the next few years because new, targeted therapies for these conditions are expected to be approved and incorporated into the class. The growing number of treatable conditions and the anticipated increase in newly diagnosed patients also will impact trend in this class.

GROWTH DEFICIENCY

Driven primarily by brand inflation, PMPY spend for growth hormone products is expected to increase in the next few years. Utilization is expected to increase marginally in 2015 and then to remain flat in 2016 and 2017, partly because utilization management programs are helping to decrease off-label use. In addition to price increases for existing medications in this class, there are no biosimilar growth hormones in the development pipeline for launch in the next few years. Some brand innovation is occurring as well. A long-acting growth hormone is on course to launch in 2015 and an oral medication, macimorelin, that is in development to diagnose growth hormone deficiency among adults, is up for FDA consideration in 2016. If approved, both may contribute to increased PMPY spend for the class.

HEMOPHILIA

The PMPY spend for medications used to treat hemophilia and other bleeding disorders is expected to increase modestly for the next few years. The forecast is based on declining utilization offset by brand inflation. With regard to price, however, a return to the doubling of price seen in the past is not expected in the next three years. Many of the most recently approved treatments are recombinant factors with increased purity, and they are expected to remain as market leaders. Although, longer-acting recombinant factors indicated for the treatment of hemophilia A and hemophilia B that were launched in 2014 are expected to capture some market share, they require less frequent dosing resulting in lower overall PMPY utilization.

Medications used to treat less-common specialty conditions, many of them orphan diseases, are forecast to increase significantly in the next few years, driven by both brand inflation and increased utilization.

PULMONARY ARTERIAL HYPERTENSION

Increases in the PMPY spend for medications used to treat pulmonary arterial hypertension (PAH) are expected in each of the next three years. Because survival rates for PAH patients are improving and they're continuing therapy longer, utilization will increase. New diagnoses of the disease are not expected to increase significantly, though, and utilization is expected to increase at a stable rate. Although generic formulations of Tracleer® (bosentan) are due in late 2015, some of the newer therapies, such as Opsumit® (macitentan), have better safety profiles and simpler dosing. As a result, the decreased prices expected from Tracleer's patent expiration are not likely to counteract brand inflation for other existing medications.

TRANSPLANT

The PMPY spend for medications used to prevent organ-transplant rejection is expected to decline even further in the next few years, making this the only specialty therapy class projected to have negative trend in each of the next three years. The expectation is based on the current 86.1% generic fill rate (GFR) for the class and the expectation of a slight decline in utilization. Although supply shortages increased costs for azathioprine in 2014, more increases are not expected to occur in the near future. In addition, Myfortic® (mycophenolic acid) and Rapamune® 0.5mg tablets (sirolimus), two of the remaining branded immunosuppressant medications, became available as generics in January 2014. No brand innovation is anticipated during the next three years.

HEREDITARY ANGIOEDEMA – A CLASS TO WATCH

The year-over-year trend forecast for specialty medications used to treat hereditary angioedema is based on the continued movement of medication billing from the medical benefits to pharmacy benefit. Changes in billing likely will be reflected as a significant increase in utilization for each of the next three years, due to improved visibility of utilization in the pharmacy benefit. Further, three new medications, including one oral drug, in the development pipeline are likely to be launched in 2017. Their releases may impact utilization, drug spend and trend for the class.

Specialty trend will slow to more sustainable levels, averaging **22.1%** over the next three years.



TREND DRIVERS



2014 PATENT EXPIRATIONS

PATENT EXPIRATION DATE	BRAND NAME (GENERIC NAME)	PRIMARY INDICATION	ESTIMATED ANNUAL SALES (MILLIONS)
Dec. 22, 2014	Vivelle-Dot® (estradiol transdermal system)	Estrogen Replacement	\$263
Dec. 11, 2014	Orapred ODT® (prednisolone sodium phosphate orally disintegrating tablets)	Anti-inflammatory	\$20
Dec. 1, 2014	Intuniv™ (guanfacine)	Attention Deficit Hyperactivity Disorder	\$668
Dec. 1, 2014	Exforge HCT® (amlodipine/valsartan/hydrochlorothiazide)	High Blood Pressure	\$158
Nov. 25, 2014	Protopic® (tacrolimus ointment)	Eczema	\$176
Nov. 20, 2014	Valcyte® (valganciclovir)	HIV	\$369
Sep. 30, 2014	Exforge® (amlodipine/valsartan)	High Blood Pressure	\$422
Sep. 8, 2014	Fortesta® (testosterone gel)	Testosterone Replacement	\$66
Sep. 3, 2014	Baraclude® (entecavir)	Hepatitis B	\$328
Aug. 27, 2014	Megace® ES (megestrol oral suspension)	Progestin	\$57
Aug. 21, 2014	Klor-Con® (potassium chloride extended-release tablets 8mEq, 10mEq)	Electrolyte Replacement	\$135
Aug. 18, 2014	Precedex™ (dexmedetomidine)	Sedative	\$156
Jun. 26, 2014	Diovan® (valsartan)	High Blood Pressure	\$2,200
Jun. 11, 2014	Testim® (testosterone gel)	Testosterone Replacement	\$266
Jun. 11, 2014	Actonel® (risedronate 150mg tablets)	Osteoporosis	\$172
Jun. 5, 2014	Oxsoralen® (methoxsalen)	Skin Conditions	\$14
May 30, 2014	Celebrex® (celecoxib)	Pain	\$2,200
May 27, 2014	Pennsaid® (diclofenac sodium topical solution 1.5%)	Pain	\$29
May 12, 2014	Exalgo® (hydromorphone extended release 8mg, 12mg, 16mg)	Pain	\$230
May 12, 2014	Rhinocort Aqua® (budesonide nasal spray)	Allergy	\$51
May 8, 2014	Astepro® (azelastine nasal spray 0.15%)	Allergy	\$97
Apr. 27, 2014	Differin® (adapalene 0.3% topical gel)	Acne	\$87
Apr. 16, 2014	Ortho Evra® (Xulane™)	Contraception	\$153
Apr. 15, 2014	Lunesta® (eszopiclone)	Insomnia	\$852
Apr. 8, 2014	Lovaza® (omega-3-acid ethyl esters)	High Blood Triglycerides	\$1,100
Apr. 1, 2014	Taclonex® (calcipotriene/betamethasone ointment)	Psoriasis	\$96
Mar. 18, 2014	Mepron® (atovaquone)	Infections	\$125
Mar. 10, 2014	Lodosyn® (carbidopa)	Parkinson's Disease	\$20

Mar. 5, 2014	Cipro® (ciprofloxacin oral suspension)	Infections	\$9
Mar. 4, 2014	Evista® (raloxifene)	Osteoporosis	\$824
Feb. 25, 2014	Micardis® HCT (telmisartan/hydrochlorothiazide)	High Blood Pressure/Heart Disease	\$209
Feb. 24, 2014	Mycobutin® (rifabutin)	Mycobacterium Avian Complex	\$19
Feb. 18, 2014	Avelox® (moxifloxacin)	Infections	\$195
Feb. 14, 2014	Boniva® Injection (ibandronate)	Osteoporosis	\$82
Feb. 5, 2014	Hectorol® (doxercalciferol capsules)	Secondary Hyperparathyroidism	\$49
Jan. 22, 2014	Bromday™ (bromfenac ophthalmic solution 0.09%)	Cataract Surgery	\$117
Jan. 14, 2014	Vanos® (fluocinonide 0.1% cream)	Dermatologicals	\$107
Jan. 8, 2014	Twynsta® (amlodipine/telmisartan)	High Blood Pressure/Heart Disease	\$7
Jan. 8, 2014	Micardis® (telmisartan)	High Blood Pressure/Heart Disease	\$274
Jan. 8, 2014	Myfortic® (mycophenolic acid delayed release tablets)	Immunosuppressant	\$307
Jan. 8, 2014	Rapamune® 0.5mg (sirolimus)	Immunosuppressant	\$12
Jan. 3, 2014	Detrol® LA (tolterodine extended release)	Overactive Bladder	\$572

HIGHLIGHTS

- On Dec. 1, 2014, Actavis announced the launch of its generic to Shire's Intuniv™ (guanfacine), one of the few non-controlled drugs used to treat attention deficit hyperactivity disorder (ADHD). It is taken once a day as monotherapy or as an add-on to stimulant medications. Actavis has 180 days of generic exclusivity, keeping competition from additional generics away until early June 2015.
- After the FDA granted 180 days of exclusivity to Ranbaxy for a generic of Genentech's Valcyte® (valganciclovir) tablets in 2008, FDA inspectors found violations at Ranbaxy's manufacturing facilities that were serious enough to ban imports of drugs from those sites. As a result, Ranbaxy was not allowed to ship generic valganciclovir, but no other generic company was allowed to produce it either. On Nov. 4, 2014, FDA reversed its approval, removed the exclusivity and allowed two companies to introduce valganciclovir in the U.S. Valganciclovir is an antiviral drug used to treat retinitis caused by cytomegalovirus (CMV) for patients with acquired immunodeficiency syndrome (AIDS), and to prevent CMV infection in certain transplant patients.
- On gaining approval from the FDA on Sep. 3, 2014, Teva Pharmaceutical Industries began shipping entecavir tablets, a generic for Bristol-Myers Squibb's Baraclude® tablets. The oral solution form of Baraclude (entecavir oral solution 0.05mg/mL) remains brand only. Entecavir is indicated for patients at least two years of age and at least 10 Kg (22 pounds) who have active hepatitis B and liver damage.
- Par Pharmaceutical Companies, Inc. announced the approval of its generics to all four strengths of Exforge® (amlodipine/valsartan — Novartis) on Sep. 30, 2014. A single pill combining a calcium channel blocker with an angiotensin II receptor blocker (ARB), Exforge was FDA approved for treating high blood pressure.
- The FDA approved TWI Pharmaceutical's generic to Megace® ES (megestrol) oral suspension 125mg/mL on Aug. 27, 2014. However the brand manufacturer, Par Pharmaceuticals, appealed the approval. Megestrol is a synthetic steroid that stimulates appetite, helping to relieve malnutrition and slow unwanted weight loss for patients with AIDS, anorexia, cancer and other conditions. It also may be used as adjunctive therapy for patients with advanced cancers of the breast, endometrium or kidneys.

The FDA approved the first generics for all four strengths (50mg, 100mg, 200mg and 400mg) of Celebrex® capsules on May 30, 2014. It is the only cyclooxygenase-2 (COX-II) inhibitor still available on the U.S. market.

- On Jun. 26, 2014, Ranbaxy finally gained full FDA approval for the generic to Novartis' Diovan® (valsartan) tablets. As the first generic to be approved, Ranbaxy gained exclusive rights to manufacture its generic version of Diovan for the first six months of generic availability when the patent first expired in September 2012. However, after receiving FDA approval, Ranbaxy's manufacturing facilities in India failed FDA inspections, so they could not produce a generic product. Due to Ranbaxy's exclusivity, no other generic company could produce valsartan either – giving Novartis nearly two extra years of full brand revenue estimated at over \$2 billion. A Ranbaxy subsidiary in the U.S., Ohm Laboratories, plans to begin shipping valsartan as soon as enough is available to supply the market.
- The FDA approved the first generics for all four strengths (50mg, 100mg, 200mg and 400mg) of Celebrex® capsules on May 30, 2014. The only cyclooxygenase-2 (COX-II) inhibitor still available on the U.S. market, celecoxib is an oral nonsteroidal anti-inflammatory drug used long term to treat osteoarthritis (OA), rheumatoid arthritis (RA) and ankylosing spondylitis. It also is used to manage acute pain in adults.
- Actavis announced on May 12, 2014, that the FDA had approved its abbreviated new drug application (ANDA) for hydromorphone extended-release tablets in 8mg, 12mg and 16mg strengths. The 32mg strength remains brand only. Neither the brand, Exalgo®, nor the new generic is abuse resistant. However, a risk evaluation and mitigation strategy (REMS) is in place.
- After settlement agreements, Dr. Reddy's, Mylan and Teva all released generics for Sunovion's Lunesta® (eszopiclone) on Apr. 15, 2014. Eszopiclone, a non-benzodiazepine sedative-hypnotic drug approved to treat insomnia, competes with several other brand and generic medications, including Ambien® (zolpidem – Sanofi, generics).

- Zydus Cadila received FDA approval for its generic to Pfizer's Rapamune® 0.5mg tablets (sirolimus) on January 8, 2014. Sirolimus is an immune-system suppressant used to prevent rejection after kidney transplants. Rapamune 1mg tablets, 2mg tablets and 1mg/mL oral solution remain brand-only. Generics to another anti-kidney transplant rejection medication, Myfortic® (mycophenolic acid delayed-release tablets), were also launched in January.

After settlement agreements, Dr. Reddy's, Mylan and Teva all released generics for Sunovion's Lunesta® (eszopiclone) on Apr. 15, 2014. Eszopiclone, a sedative-hypnotic drug approved to treat insomnia, competes with several other brand and generic medications, including Ambien® (zolpidem – Sanofi, generics).

BRAND APPROVALS

APPROVAL OR ACTION DATE	BRAND (GENERIC NAME)	PRIMARY INDICATION	PRODUCT UNIQUENESS
Dec. 23, 2014	Dyloject™ (diclofenac sodium injection)	Pain	Existing product with new dosing form
Dec. 23, 2014	Namzaric™ (memantine/donepezil)	Alzheimer's Disease	New combination of existing products
Dec. 23, 2014	Saxenda® (liraglutide)	Obesity	Existing product with new dosing form
Dec. 22, 2014	Opdivo® (nivolumab)	Melanoma	Similar to existing products
Dec. 19, 2014	Rapivab™ (peramivir)	Influenza	Similar to existing products
Dec. 19, 2014	Zerbaxa™ (ceftolozane/tazobactam)	Infections	Similar to existing products
Dec. 19, 2014	Soolantra® (ivermectin 1% cream)	Rosacea	Existing product with new dosing form
Dec. 19, 2014	Viekira Pak™ (ombitasvir/paritaprevir/ritonavir/dasabuvir)	Hepatitis C	Similar to existing products
Dec. 19, 2014	Lynparza™ (olaparib)	Ovarian Cancer	New mechanism of action
Dec. 17, 2014	Xtoro™ (finafloxacin otic suspension)	Otitis Externa	Similar to existing products
Dec. 15, 2014	Signifor® LAR (pasireotide long acting)	Acromegaly	Existing product with new dosing form
Dec. 5, 2014	Trezix™ (acetaminophen/cafeine/dihydrocodeine)	Pain	New combination of existing products
Dec. 3, 2014	Blincyto™ (blinatumomab)	Cancer	New mechanism of action
Nov. 25, 2014	Onexton™ (clindamycin/benzoyl peroxide gel)	Acne	New combination of existing products
Nov. 20, 2014	Hysingla™ ER (hydrocodone)	Pain	Existing product with new dosing form
Nov. 14, 2014	Lemtrada™ (alemtuzumab)	Multiple Sclerosis	Refinement of an existing product
Nov. 14, 2014	Obredon™ (hydrocodone/guaifenesin)	Cough, Colds	New combination of existing products
Oct. 29, 2014	Xigduo™ XR (dapagliflozin/metformin)	Diabetes	New combination of existing products
Oct. 23, 2014	Obizur (antihemophilic factor [recombinant], porcine sequence)	Acquired Hemophilia A	Similar to existing products
Oct. 22, 2014	Sotylize™ (sotalol oral solution)	Arrhythmia	Existing product with new dosing form
Oct. 15, 2014	Ofev® (nintedanib)	Idiopathic Pulmonary Fibrosis	New mechanism of action
Oct. 15, 2014	Esbriet® (pirfenidone)	Idiopathic Pulmonary Fibrosis	New mechanism of action
Oct. 10, 2014	Akynzeo® (netupitant/palonosetron)	Nausea	New mechanism of action
Oct. 10, 2014	Harvoni® (ledipasvir/sofosbuvir)	Hepatitis C	New mechanism of action
Sep. 26, 2014	Iluvien™ (fluocinolone intravitreal implant)	Diabetic Macular Edema	Similar to existing products
Sep. 25, 2014	Vitekta™ (elvitegravir)	HIV	New combination of existing products
Sep. 25, 2014	Tybost® (cobicistat)	HIV	Existing product with new dosing form
Sep. 24, 2014	Spiriva® Respimat® (tiotropium)	COPD	Existing product with new dosing form
Sep. 18, 2014	Trulicity™ (dulaglutide)	Diabetes	Similar to existing products
Sep. 16, 2014	Movantik™ (naloxegol)	Opioid-Induced Constipation	Similar to existing products

Sep. 12, 2014	HyQvia (immune globulin/hyaluronidase)	Primary Immunodeficiency	Refinement of an existing product
Sep. 10, 2014	Contrave® (naltrexone/bupropion)	Weight Loss	New combination of existing products
Sep. 4, 2014	Keytruda® (pembrolizumab)	Metastatic Melanoma	New mechanism of action
Aug. 22, 2014	Triumeq® (abacavir/dolutegravir/lamivudine)	HIV	New combination of existing products
Aug. 20, 2014	Arnuity™ Ellipta® (fluticasone furoate)	Asthma	Refinement of an existing product
Aug. 19, 2014	Cerdelga™ (eliglustat)	Gaucher Disease	New mechanism of action
Aug. 15, 2014	Plegridy™ (peginterferon beta-1a)	Multiple Sclerosis	Refinement of an existing product
Aug. 13, 2014	Belsomra® (suvorexant)	Insomnia	New mechanism of action
Aug. 8, 2014	Invokamet™ (canagliflozin/metformin)	Diabetes	New combination of existing products
Aug. 6, 2014	Orbactiv™ (oritavancin)	Infections	New mechanism of action
Aug. 1, 2014	Jardiance® (empagliflozin)	Diabetes	New mechanism of action
Jul. 31, 2014	Striverdi® Respimat® (olodaterol)	COPD	New mechanism of action
Jul. 23, 2014	Acticlate® (doxycycline hyclate)	Acne	Existing product with new dosing form
Jul. 23, 2014	Zydelig® (idelalisib)	Cancer	New mechanism of action
Jul. 23, 2014	Targiniq™ ER (oxycodone extended release/naloxone)	Pain	Existing product with new dosing form
Jul. 16, 2014	Ruconest® (C1 esterase inhibitor [recombinant])	Hereditary Angioedema	Similar to existing products
Jul. 22, 2014	Ryanodex® (dantrolene)	Malignant Hyperthermia	Existing product with new dosing form
Jul. 10, 2014	Rasuvo® (methotrexate auto-injector)	Inflammatory Conditions	Existing product with new dosing form
Jul. 7, 2014	Kerydin™ (tavaborole)	Toenail Fungus	Similar to existing products
Jul. 3, 2014	Beleodaq™ (belinostat)	Cancer	New mechanism of action
Jun. 27, 2014	Vazculep™ (phenylephrine)	Low Blood Pressure	Refinement of an existing product
Jun. 27, 2014	Afrezza® (inhaled insulin)	Diabetes	Existing product with new dosing form
Jun. 20, 2014	Sivextro® (tedizolid)	Antibacterial	Similar to existing products
Jun. 6, 2014	Eloctate™ (antihemophilic factor [recombinant], Fc fusion protein)	Hemophilia A	Similar to existing products
Jun. 6, 2014	Bunavail™ (buprenorphine/naloxone buccal film)	Opioid Dependence	New combination of existing products
Jun. 6, 2014	Jublia® (efinaconazole topical solution)	Toenail Fungus	Similar to existing products
Jun. 4, 2014	Vogelxo™ (testosterone nasal gel)	Testosterone Replacement	Existing product with new dosing form
May 30, 2014	Omidria™ (phenylephrine/ketorolac injection)	Eye Surgery	New combination of existing products
May 28, 2014	Natesto™ (testosterone nasal gel)	Testosterone Replacement	Existing product with new dosing form
May 23, 2014	Dalvance™ (dalbavancin)	Antibiotic	Similar to existing products
May 22, 2014	QVAR® with Dose Counter (beclomethasone aerosol)	Asthma	Refinement of an existing product
May 19, 2014	Entyvio® (vedolizumab)	Inflammatory Bowel Disease	New mechanism of action
May 8, 2014	Zontivity™ (vorapaxar)	Antiplatelet	New mechanism of action
May 5, 2014	Epanova® (omega-3-carboxylic acids)	High Cholesterol	Similar to existing products

Apr. 30, 2014	Incruse™ Ellipta® (umeclidinium)	COPD	Similar to existing products
Apr. 29, 2014	Zykadia™ (ceritinib)	Lung Cancer	Similar to existing products
Apr. 28, 2014	Purixan™ (mercaptopurine oral suspension)	Cancer	Existing product with new dosing form
Apr. 22, 2014	Sylvant™ (siltuximab)	Castleman's Disease	New mechanism of action
Apr. 21, 2014	Cyramza® (ramucirumab)	Gastric Cancer	Similar to existing products
Apr. 17, 2014	Ragwitek® (short ragweed pollen allergen extract)	Allergy	Similar to existing products
Apr. 15, 2014	Tanzeum™ (albiglutide)	Diabetes	Similar to existing products
Apr. 14, 2014	Grastek® (Timothy grass pollen allergen extract)	Allergy	Similar to existing products
Apr. 3, 2014	Evzio™ (naloxone autoinjector)	Opioid Overdose	Existing product with new dosing form
Apr. 1, 2014	Oralair® (mixed grass pollens allergen extract)	Allergy	New mechanism of action
Mar. 28, 2014	Alprolix® (coagulation factor IX [recombinant] Fc Fusion protein)	Hemophilia B	Similar to existing products
Mar. 24, 2014	Metronidazole 1.3% Vaginal Gel (metronidazole 1.3% vaginal gel)	Infection	Refinement of an existing product
Mar. 21, 2014	Otezla® (apremilast)	Psoriatic Arthritis	New mechanism of action
Mar. 19, 2014	Impavido® (miltefosine)	Leishmaniasis	New mechanism of action
Mar. 14, 2014	Hemangeol™ (propranolol oral solution)	Infantile Hemangioma	Existing product with new dosing form
Mar. 13, 2014	Noxafil® (posaconazole)	Fungal Infection	Similar to existing products
Mar. 11, 2014	Qudexy™ XR (topiramate)	Seizures	Existing product with new dosing form
Mar. 11, 2014	Xartemis™ XR (oxycodone/acetaminophen)	Pain	Similar to existing products
Mar. 5, 2014	Aveed® (testosterone undecanoate)	Hypogonadism	Similar to existing products
Feb. 24, 2014	Tivorbex™ (indomethacin)	Pain	Refinement of an existing product
Feb. 24, 2014	Myalept™ (metreleptin)	Generalized Lipodystrophy	New mechanism of action
Feb. 18, 2014	Northera™ (droxidopa)	Neurogenic Orthostatic Hypotension	New mechanism of action
Feb. 14, 2014	Vimizim® (elosulfase alfa)	Morquio A Syndrome	New mechanism of action
Jan. 31, 2014	Hetlioz® (tasimelteon)	Non-24-Hour Sleep-Wake Disorder	Similar to existing products
Jan. 16, 2014	Pennsaid® 2% (diclofenac topical solution 2%)	Pain/Inflammation	Refinement of an existing product
Jan. 8, 2014	Farxiga™ (dapagliflozin)	Diabetes	Similar to existing products

HIGHLIGHTS

- Bristol-Myers Squibb received accelerated approval from the U.S. Food and Drug Administration (FDA) on Dec. 22, 2014 for its breakthrough cancer therapy, Opdivo® (nivolumab). A human programmed death receptor-1 (PD-1)-blocking antibody, it is indicated for the treatment of patients with unresectable or metastatic melanoma that has progressed despite treatment with Yervoy® (ipilimumab – Bristol-Myers Squibb).
- On Dec. 19, 2014, AbbVie received FDA approval of Viekira Pak™ (ombitasvir/paritaprevir/ritonavir tablets co-packaged with dasabuvir) for the treatment of chronic hepatitis C virus (HCV) genotype 1 infection. Viekira Pak contains three new antivirals: ombitasvir, an NS5a inhibitor; paritaprevir, a protease inhibitor; and dasabuvir, a non-nucleoside polymerase inhibitor. Ritonavir, also a protease inhibitor, is used as a “booster” to increase the effects of paritaprevir.
- AstraZeneca’s Lynparza™ (olaparib) received FDA approval on Dec. 19, 2014. It is indicated as monotherapy to treat patients with advanced ovarian cancer that has or is suspected to have deleterious germline BRCA mutations (gBRCAm). Because the specific mutations must be confirmed by an FDA-approved test before Lynparza treatment is initiated, the FDA also approved Myriad Genetics’ BRACAnalysis CDx™. It is a companion diagnostic blood test that identifies the 10% to 15% of ovarian cancers carrying the mutations. Additionally, to be eligible to use Lynparza, patients must have already been treated with at least three other types of chemotherapy.
- The FDA announced its approval of Purdue Pharma’s Hysingla™ ER, a controlled-release form of hydrocodone, on Nov. 20, 2014. Taken once every 24 hours, it is indicated to manage pain that is severe enough to require continuous, long-term opioid treatment and that has not been controlled by prior therapy. At the time of its approval, Hysingla ER was the only abuse-deterrent, single-agent hydrocodone product approved in the U.S.

On Dec. 19, 2014, AbbVie received FDA approval of Viekira Pak™ (ombitasvir/paritaprevir/ritonavir and dasabuvir) for the treatment of chronic hepatitis C virus (HCV) genotype 1 infection.

- On Nov. 14, 2014, Genzyme, a Sanofi company, received FDA approval for Lemtrada™ (alemtuzumab) to treat relapsing forms of multiple sclerosis (MS). It will be third-line therapy for patients whose condition has not responded to two or more other MS therapies. Because it has the potential for very severe side effects, Lemtrada’s prescribing and dispensing is restricted to certified providers. In the U.S., alemtuzumab originally was approved in 2001 (under the brand name Campath®) for treating chronic lymphocytic leukemia. Its marketing for the cancer indication was terminated by the manufacturer in Sept. 2012.
- On Oct. 15, 2014, the FDA approved Esbriet® (pirfenidone – Genentech) and Ofev® (nintedanib – Boehringer Ingelheim), the first two drugs to treat idiopathic pulmonary fibrosis (IPF). A fatal lung disease, IPF progressively scars the lungs, eventually ending their ability to absorb oxygen. Approximately 100,000 Americans, mostly older men, have IPF. The median survival time from diagnosis is only two years to five years, and the five-year survival rate is less than 40%. Before the approvals of Esbriet and Ofev, the only therapies for IPF were breathing treatments, supplemental oxygen and lung transplants.
- Gilead received FDA approval on Oct. 10, 2014, for Harvoni® (ledipasvir/sofosbuvir) tablets to treat adults with genotype 1 chronic hepatitis C virus (HCV). Launched within days of approval, Harvoni is a single tablet that contains Gilead’s Sovaldi® (sofosbuvir) and ledipasvir, the first FDA-approved drug in a new class known as NS5a inhibitors. Harvoni is taken once daily, with no need for patients to use ribavirin or interferon. It is priced at \$1,125 per tablet.
- On Sept. 4, 2014, Merck received accelerated approval from the FDA for its breakthrough therapy Keytruda® (pembrolizumab). It was the first FDA-approved human programmed death receptor-1 (PD-1) blocking antibody. Keytruda is indicated for the treatment of inoperable or metastatic melanoma that has progressed despite treatment with Yervoy® (ipilimumab – Bristol-Myers Squibb). If the cancer is positive for BRAF V600 mutations, a BRAF inhibitor, such as Tafinlar® (dabrafenib – GlaxoSmithKline) also must be tried first.
- The FDA approved Contrave® (naltrexone/bupropion) extended-release tablets on Sept. 10, 2014. Contrave is indicated for chronic weight management in addition to reduced-calorie diet and exercise. It is approved for use by adults who are obese – those

with an initial body mass index (BMI) of 30 Kg/m² or higher. Adults with BMIs between 27 Kg/m² and 30Kg/m² and with one or more weight-related conditions, such as high blood pressure, type 2 diabetes or high cholesterol, also are candidates for its use.

- The FDA approved Jardiance® (empagliflozin) on Aug. 1, 2014. Along with diet and exercise, Jardiance is indicated to improve blood sugar control for adults with type 2 diabetes. Jardiance is the third sodium-glucose co-transporter 2 (SGLT2) inhibitor to be approved in the U.S. Invokana® (canagliflozin – Janssen) was approved in March 2013 and Farxiga™ (dapagliflozin – AstraZeneca) followed in Jan. 2014.
- Biogen Idec announced on Aug. 15, 2014, that the FDA had approved Plegridy™ (peginterferon beta-1a) to treat relapsing forms of multiple sclerosis (MS). Plegridy is a pegylated formulation of the same drug in Biogen's Avonex®. However, pegylation allows the medication to stay in the body longer, so Plegridy needs to be administered only once every two weeks, compared to once weekly for Avonex. Additionally, Plegridy is injected subcutaneously (subQ), which generally is less painful and easier for patients to self-administer than the intramuscular (IM) injections needed for Avonex.
- After two previous tries, MannKind's inhaled insulin, Afrezza® (insulin human) inhalation powder won FDA approval on June 27, 2014, for treating adults with diabetes, either type 1 or type 2.
- The FDA approved Biogen Idec's Eloctate™ (antihemophilic [recombinant], Fc fusion protein) on June 6, 2014. Eloctate is indicated to control and prevent bleeding episodes, manage bleeding during surgical procedures and prevent or reduce bleeding episodes in adults and children with hemophilia A. It lasts longer in the body than other antihemophilia factors, so it can be dosed less often for prevention.
- Greer Laboratories announced on April 1, 2014, that the FDA had approved Oralair® (mixed grass pollens allergens extract). The first FDA-approved sublingual immunotherapy (SLIT) agent for allergies in the U.S., it contains pollen extracts from a variety of grasses. Approval for a second SLIT, Grastek® (Timothy grass pollen extract – Merck), followed two weeks later. And a third, Ragwitek® (short ragweed pollen allergen extract – Merck), was approved on April 17, 2014. These new SLIT drugs may replace allergy shots for some patients.

- On April 3, 2014, the FDA approved a one-use naloxone auto-injector for emergency treatment of known or suspected opioid overdose. Evzio™ (naloxone injection) is to be used by caregivers as soon as signs of an opioid overdose are suspected. Each Evzio dose is prepackaged in a small container on which clearly written and pictured directions for use appear. The package also includes a speaker that delivers audible step-by-step instructions for use.
- On March 11, 2014, the FDA gave Mallinckrodt approval for Xartemis™ XR Extended-Release Capsules (C-II), the first extended-release formulation of oxycodone and acetaminophen. It is indicated for managing severe acute pain requiring an opioid, after previous treatment options have been inadequate.
- After priority review, the FDA approved Hetlioz™ (tasimelteon) capsules on Jan. 31, 2014. Hetlioz is the first treatment for Non-24-Hour Sleep-Wake Disorder (Non-24). A chronic circadian rhythm disorder, Non-24 keeps patients from aligning their body clocks with the 24-hour day-night cycle. Most totally blind patients (about 80,000 in the U.S.) have Non-24, which disrupts sleep and causes stress that often results in social and occupational problems.

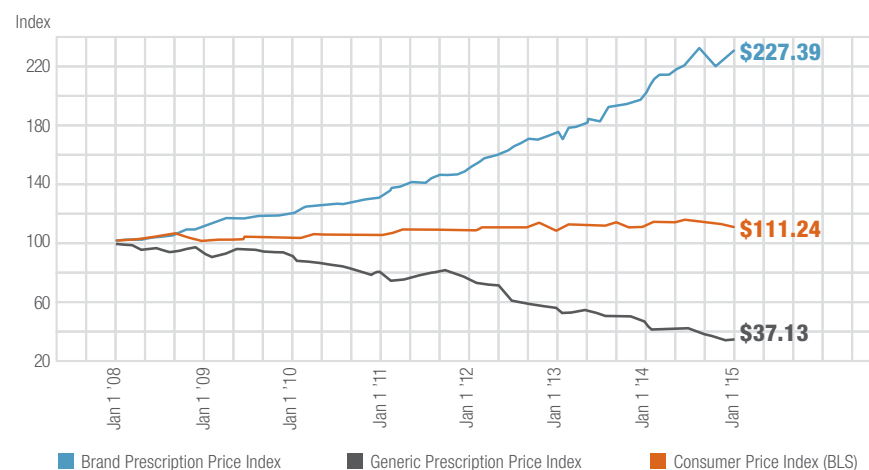
On Oct. 15, 2014, the FDA approved Esbriet® (pirfenidone – Genentech) and Ofev® (nintedanib – Boehringer Ingelheim), the first two drugs to treat idiopathic pulmonary fibrosis (IPF). A fatal lung disease, IPF progressively scars the lungs, eventually ending their ability to absorb oxygen. Approximately 100,000 Americans, mostly older men, have IPF.

THE EXPRESS SCRIPTS PRESCRIPTION PRICE INDEX

Compared to the prices of generic drugs and drugs a year earlier, in December 2014 generic drug prices were 20.0% lower, whereas brand prices were 15.4% higher. The magnitude of change in generic drug prices has decreased since 2013, following the dramatic deflation seen in 2012 – when billions of dollars’ worth of brand blockbuster medications lost patent protection in what was dubbed “the patent cliff,” paving the way for unprecedented generic competition. In addition, price increases for several commonly used generics have had an offsetting effect, contributing to a slowing of the decline in prices. This isolated inflation in generic-drug pricing is related to a range of market factors, such as fewer manufacturers of those generics and shortages of active ingredients. Even so, generic medications overall continue to deliver significant savings over brand-name alternatives.

The gap between brand inflation and generic deflation has increased slightly, from 29.8 percentage points in December 2013 to 35.5 percentage points in December 2014. From the base price of \$100.00 set in January 2008, in December 2014 prices for the most commonly used generic medications decreased to \$37.13 (in 2008 dollars), and prices for the most commonly used brand medications increased to \$227.39 (in 2008 dollars). In contrast, a market basket of commonly used household goods costing \$100.00 in 2008, as measured by the Bureau of Labor Statistics (BLS) Consumer Price Index, grew to only \$111.24 (in 2008 dollars) by December 2014.

THE EXPRESS SCRIPTS PRESCRIPTION PRICE INDEX





MEDICARE

MEDICARE YEAR IN REVIEW

In 2014, for the second year in a row, Medicare saw booming growth. Two million more Americans became eligible for the federal program, bringing the number of Medicare Part D beneficiaries to 37 million.¹⁹ At the same time, Medicare plan sponsors faced the ongoing challenge of maintaining costs and quality for a growing population while remaining compliant with Centers for Medicare & Medicaid Services (CMS) requirements.

Express Scripts' Medicare plans faced stiff competition as a result of considerable downward pressure on beneficiary premiums and copayments. Plans also faced higher-than-ever stakes around CMS's Star Ratings. The end of the Quality Bonus Payment Demonstration, along with continued shifts in regulation parameters for adherence and diabetes treatments, increased this pressure. The industry also witnessed steep inflation for compounded ingredients. The most challenging issue for Medicare plans in 2014, however, was the management of the skyrocketing trend for specialty drugs, driven primarily by new, expensive treatments for hepatitis C.

To manage these diverse challenges and remain competitive, several trends were common among Medicare Part D plans in 2014:

- Adoption of a more aggressive benefit design and a tightly managed formulary
- An increase in the number of plans offering five-tier cost-sharing structures
- A rapid increase in the number of Prescription Drug Plan (PDP) plan sponsors using preferred pharmacy networks, allowing penetration to reach 72%

WHAT'S DRIVING MEDICARE DRUG TREND

The total spend for Medicare plans rose 13.8% in 2014, to \$2,987.36, as a result of a modest increase in utilization (0.5%) combined with a significant increase in unit costs (13.3%). Traditional drug spend increased 6.4%, driven by relatively stable utilization and a 5.9% increase in unit costs. Although specialty medications represented only about one-quarter of total Medicare drug spend, their contribution to trend was significant: specialty spend increased 45.9% in 2014, following a much more modest increase of 14.7% in 2013.

The total spend for Medicare plans rose **13.8%** in 2014, as a result of a modest increase in utilization combined with a significant increase in unit costs.

Specialty Utilization and Hepatitis C

Perhaps the largest impact for Medicare plan sponsors in 2014 arose as a result of new, expensive treatments for hepatitis C, namely Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir). After the approval and marketplace launch of Sovaldi and Olysio in late 2013, treatment guidelines were quickly updated to recommend the use of these novel agents in the treatment of patients with hepatitis C (genotype 1), instead of older treatments on the market.²⁰ Harvoni became available in October 2014.

Treatment with one of these three new drugs is among the most-expensive therapeutic regimens available, with the cost of a course of therapy as high as \$150,000. Plan sponsors spent an average of \$102.83 per-member-per-year (PMPY) on these three drugs alone in 2014 – more than the PMPY cost for the entire class of inflammatory drugs that treat more common conditions, such as rheumatoid arthritis and psoriasis. In contrast, sponsors of Express Scripts commercial plans spent only \$37.95 PMPY for all hepatitis C drugs in 2014.



The reason for this disparity is that – unlike commercial health plans, which could use utilization-management tools such as prior authorization and even formulary placement to manage the costs of these expensive new drugs – without prior CMS approval, Medicare health plans could not remove the new drugs from their 2014 formularies mid-year, hampered from taking proper advantage of innovative cost-containment solutions that commercial clients employed successfully. Medicare health plans witnessed a dramatic increase in specialty drug spend.

Looking ahead, however, Medicare plans can expect improved trend in 2015 as plan sponsors successfully leverage more utilization-management tools for these drugs, such as prior authorization criteria. This is welcome news for plan sponsors and the Part D industry, as the impact of these new hepatitis C drug therapies will be felt more fully in 2015 and beyond.

The Pharmacy Care Management Association (PCMA) and Milliman have estimated that new therapies, including Sovaldi and Olysio, will increase Medicare Part D federal spending by \$2.9 billion to \$5.8 billion in 2015.²¹ Viekira Pak™, another breakthrough hepatitis C treatment, was added to Express Scripts formularies for commercially insured plan sponsors and, as of January 1, 2015, is the exclusive option for those plans' patients with genotype 1 hepatitis C, regardless of symptoms or disease progression.

Quality and Star Ratings Measures

CMS continues to emphasize the importance of clinical-outcome measures through the Medicare Part D Star Rating system. The financial benefits of the highest rated 4-Star or 5-Star plan ratings are key for plans' long-term solvency and competitiveness.

Even though the financial incentives that encourage better adherence are aligned with Medicare Advantage Part D (MAPD) plans, 2014 was the first year in which Part D plan sponsors also demonstrated an overall market improvement in Star Rating measures related to adherence. Still, better adherence came with the added cost that naturally ensues from the use of more prescription drugs. Medicare plan sponsors were focused on achieving the increasingly difficult 5-Star threshold for diabetes treatments and the three adherence measures – measures that are particularly hard to maintain and even more difficult to improve. For instance, the 2015 5-Star adherence threshold for cholesterol medication adherence will increase to 83% in 2015, from 75% in 2014. The anticipation of these types of shifts in Star Rating measures caused Medicare plan sponsors to implement more aggressive and creative clinical solutions in 2014 to drive greater member adherence, a trend whose success played out in Medicare spend and utilization increases.

The hypertension measures provided a particularly complex Star Ratings challenge in 2014. In February 2014, the Eighth Joint National Committee (JNC 8) released starkly different guidelines for the treatment of hypertension,²² a prevalent condition affecting an estimated 58% of Medicare beneficiaries.²³ The changed guidelines still advocate tight management of high blood pressure in certain patients, but they now recommend that adults over the age of 75 with chronic kidney disease not be treated for hypertension with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB). The use of diuretics, calcium channel blockers (CCB) and beta blockers, when appropriate, is still recommended.

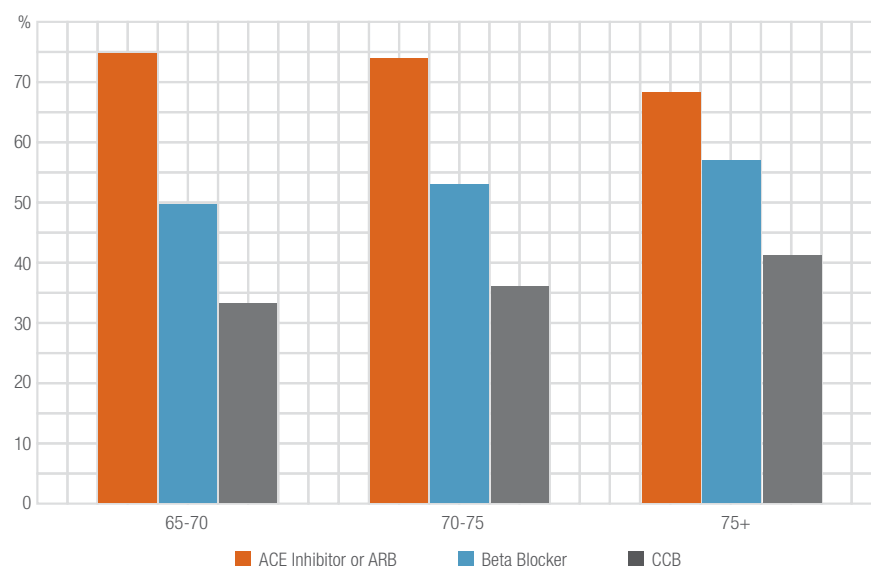
Industry research estimates new therapies for hepatitis C, including Sovaldi® and Olysio®, will increase Medicare Part D federal spending by \$2.9 billion to \$5.8 billion in 2015.

However, the specifications from which CMS draws evidence for *current* Star Ratings use treatment guidelines issued in 2003. The Pharmacy Quality Alliance (PQA) decided in January 2015 to retire the Star Ratings measure related to appropriate treatment of hypertension in patients with diabetes, and this retired measure reflected pre-JNC 8 recommendations.

Data from an exclusive Express Scripts study looked at pharmacy claims for nearly 2.4 million Medicare patients in 2013. The data suggested that the JNC 8 guideline changes are consistent with how physicians are already treating older patients with hypertension. The percentage of Medicare beneficiaries who filled a prescription for an ACE inhibitor or an ARB *declined* with age, while the use of calcium channel blockers and beta blockers *increased* (see chart below). Part D plans now have research to support the prescribing trends seen and, as such, should be encouraged to continue monitoring prescribing pattern changes that fall in line with updates to treatment guidelines.

PERCENT OF MEDICARE BENEFICIARIES USING HIGH BLOOD PRESSURE MEDICATIONS

BY AGE GROUP



Following all of this industry dialogue, in February's 2016 Draft Call Letter, CMS announced it would retire the Part D Diabetes Treatment measure for CY 2017 Star Ratings. This measure will still be included in the 2016 Star Ratings, based on plan sponsors' 2014 data. However, going forward the Diabetes Treatment measure will not impact Star Ratings performance. Medicare plans should seek to understand the impact of this change within their broader Star Ratings strategy and clinical approach.

SOLUTIONS FOR MEDICARE'S CHALLENGES

To address plans' Star Ratings challenges, Express Scripts offers a range of clinical solutions to boost Part C and Part D performance. Plans wanting to improve clinical Star measures benefit from our highly specialized solutions that align programs for pharmacists, physicians, patients and case managers, and help drive optimal performance against plans' pharmacy measures *and* medical measures. Because client needs are unique, our menu of Stars Solutions is deep – including ScreenRx®, which uses predictive modeling and tailored interventions to drive adherence; RationalMed®, which uses proprietary clinical analysis of prescription, medical and laboratory data to identify safety risks; and solutions that target diabetes-treatment initiatives and support prescribing-physician best practices.

The clinically specialized Therapeutic Resource Centers (TRCs) of the Express Scripts Pharmacy and Accredo Specialty Pharmacy deliver superior treatment outcomes and cost-effectiveness by supporting patients through the challenges of complex and costly diseases. Our specialist pharmacists and nurses each receive clinically specialized training in one disease state, and the work they do focuses almost exclusively on that clinical condition. This specialized expertise and commitment enables an optimal patient experience and ensures the highest performance in pharmacy safety, improved medication adherence and closing gaps in care. With their highly specialized knowledge of the complex disease states and complicated treatment protocols they manage, these TRC pharmacists and nurses often have more experience in rare conditions than some of the physicians who prescribe the treatments.

In addition, the adherence benefits for Medicare members who choose the Express Scripts Pharmacy for home delivery of prescription medications are well documented. A growing body of evidence suggests that the choice of where Medicare beneficiaries fill their medications is vitally linked to adherence success.

In 2014, Express Scripts conducted the first known, well-controlled, head-to-head comparison of prescriptions dispensed at retail pharmacies and at home delivery pharmacies. The peer-reviewed study, which controlled for socioeconomic status and excluded patients using home delivery automatic refill programs, examined 29 million de-identified claims corresponding to nearly 1 million Medicare beneficiaries taking medication for diabetes, high blood pressure or high cholesterol over a two-year period. The study found that beneficiaries who receive medication for diabetes, high blood pressure and high cholesterol via home delivery pharmacy are between 25% and 29% more likely to be adherent to prescription drug therapy than patients with these conditions who fill their prescriptions at a retail pharmacy.²⁴ Programs like MyRxChoices® are designed to educate members on the benefits of home delivery pharmacy and thus maximize the adherence performance benefits to plans.

Medicare beneficiaries who receive medication for diabetes, high blood pressure and high cholesterol via home delivery pharmacy are between **25%** and **29%** more likely to adhere to prescription drug therapy than patients with these conditions who fill their prescriptions at a retail pharmacy.²⁴

A LOOK AT MEDICARE OVERALL DRUG TREND FOR 2014

We further examined Medicare trend in 2014 by Medicare plan type: Medicare Advantage Part D (MAPD), Prescription Drug Plan (PDP) and Employer Group Waiver Plan (EGWP). Traditional spend for MAPDs increased 7.0%, with a member-per-year (PMPY) spend of \$1,751.11, stemming from a 6.1% increase in unit cost combined with a 0.9% increase in utilization. The specialty PMPY spend for MAPDs in 2014 increased to \$542.05, a 43.3% increase over 2013.

EGWPs, which comprise plan sponsors that continue to offer benefits to their retirees, tend to have broader formularies, lower copayments and fewer member restrictions. In 2014, EGWP plans had the highest PMPY spend (\$2,800.49) for traditional drugs among the three Medicare plan types, but they also had a slightly lower increase in utilization for traditional drugs than both MAPD and PDP plans. For specialty drugs, EGWPs had a 33.9% increase to \$738.25 PMPY spend.

Medicare traditional drug spend increased 8.6%, to \$2,403.49, for PDP plans, driven largely by a 7.6% increase in unit cost. In addition, PDP plans had a higher specialty spend increase (60.0%) than the two other types of Medicare plans.

Overall, we saw the impact of benefit design driving significant differences in MAPD, PDP and EGWP trend. For example, we saw PDP members' increased adherence in two measures (D12-blood pressure medication adherence and D13-cholesterol medication adherence), which was reflected in higher PMPY spend and utilization for these commonly used medications than MAPDs experienced. Again, richer plan designs are associated with PDPs, whereas EGWPs are driving higher PMPY spend. However, we will be closely watching this trend in 2015 and beyond, because PDP and EGWP plan designs are now changing to include more tightly managed benefit designs and closed formulary options.

COMPONENTS OF MEDICARE TREND

2014

	PMPY SPEND	TREND		
		UTILIZATION	UNIT COST	TOTAL
Traditional	\$2,262.41	0.5%	5.9%	6.4%
Specialty	\$724.94	11.6%	34.3%	45.9%
TOTAL OVERALL	\$2,987.36	0.5%	13.3%	13.8%

January-December 2014 compared to same period in 2013

MAPD

	PMPY SPEND	TREND		
		UTILIZATION	UNIT COST	TOTAL
Traditional	\$1,751.11	0.9%	6.1%	7.0%
Specialty	\$542.05	9.1%	34.2%	43.3%
TOTAL OVERALL	\$2,293.16	1.0%	12.9%	13.9%

January-December 2014 compared to same period in 2013

PDP

	PMPY SPEND	TREND		
		UTILIZATION	UNIT COST	TOTAL
Traditional	\$2,403.49	1.0%	7.6%	8.6%
Specialty	\$872.89	18.5%	41.5%	60.0%
TOTAL OVERALL	\$3,276.38	1.1%	17.7%	18.8%

January-December 2014 compared to same period in 2013

EGWP

	PMPY SPEND	TREND		
		UTILIZATION	UNIT COST	TOTAL
Traditional	\$2,800.49	0.8%	6.0%	6.8%
Specialty	\$738.25	11.2%	22.7%	33.9%
TOTAL OVERALL	\$3,538.74	0.8%	10.6%	11.5%

January-December 2014 compared to same period in 2013

MEDICARE: TRADITIONAL THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 MEDICARE TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Diabetes	\$358.93	4.9%	21.5%	26.4%
2	High Blood Cholesterol	\$205.70	0.3%	-1.3%	-1.0%
3	Pain/Inflammation	\$196.26	-1.4%	10.4%	9.1%
4	High Blood Pressure/Heart Disease	\$184.93	0.1%	-11.2%	-11.1%
5	Mental/Neurological Disorders	\$183.18	-3.0%	7.3%	4.2%
6	Asthma	\$130.51	2.6%	-0.2%	2.4%
7	Heartburn/Ulcer Disease	\$113.11	0.0%	-4.1%	-4.1%
8	Depression	\$71.95	1.5%	-20.2%	-18.7%
9	Urinary Disorders	\$71.29	3.4%	0.5%	3.9%
10	Anticoagulants	\$57.22	4.2%	56.1%	60.2%
TOTAL TRADITIONAL		\$2,262.41	0.5%	5.9%	6.4%

Diabetes saw a higher PMPY spend **(\$358.93)** than any other traditional therapy class among Medicare beneficiaries.

Together, the top three Medicare traditional therapy classes ranked by per-member-per-year (PMPY) spend – diabetes, high blood cholesterol and pain/inflammation – contributed 33.6% of total PMPY spend for all traditional medications used by Medicare beneficiaries in 2014. Total traditional trend was 6.4%, mainly the result of increased unit costs.

HIGHLIGHTS

- Diabetes saw a higher PMPY spend (\$358.93) than any other traditional therapy class among Medicare beneficiaries. Trend for diabetes medications was 26.4%, driven by a small increase in utilization (4.9%) and a significant increase in unit cost (21.5%). Highly utilized medications with double-digit increases in unit-cost trend, including Lantus® (insulin glargine [rDNA origin]) and Januvia® (sitagliptin), are driving spend in this therapy class. Invokana® (canagliflozin), the first in a relatively new class of diabetes treatments known as sodium-glucose co-transporter 2 (SGLT2) inhibitors, experienced a substantial increase in utilization after gaining exposure in the market. Two other SGLT2 inhibitors, Farxiga™ (dapagliflozin) and Jardiance® (empagliflozin), were approved in 2014. Competition among them is likely to have an impact on trend in 2015.
- Total PMPY spend for medications used to treat pain and inflammation increased 9.1%, despite a slight drop in utilization. Some of the most commonly used medications in this therapy class – including Celebrex® (celecoxib), the only available COX-2 inhibitor – had double-digit increases in unit-cost trend. For Celebrex, the increase was likely related to the manufacturer's profit-protection efforts, stemming from the drug's patent expiration in June 2014.
- In 2014, the trends for both high blood pressure/heart disease medications and depression medications were negative. Declines in unit costs attributed to the genericization of these classes were responsible. In 2014, the generic fill rate (GFR) for the high blood pressure/heart disease class increased to 96.2%, while the GFR for depression treatments increased to 97.4%.
- The double-digit increase in unit cost for traditional anticoagulant medications was primarily driven by unit-cost increases for Xarelto® (rivaroxaban) and Eliquis® (apixaban). Both drugs also experienced significant increases in utilization, likely as a result of patients switching from less-convenient warfarin and specialty injectable anticoagulants. Overall trend for the class was 60.2%.

In 2014, the generic fill rate (GFR) for the high blood pressure/heart disease class increased to **96.2%**, while the GFR for depression treatments increased to **97.4%**.

TOP 10 MEDICARE TRADITIONAL DRUGS

Three of the top 10 most-expensive traditional drugs when ranked by Medicare per-member-per-year (PMPY) spend – Lantus, Januvia and Levemir – are indicated to treat diabetes. Together, these three drugs contributed 6.7% of all Medicare traditional drug spend in 2014. Individuals age 65 and older are almost twice as likely to have diagnosed diabetes as younger individuals.²⁵ Brand drugs dominated the top 10 drugs, with the sole generic, duloxetine, ranking in ninth place. Total trend was highest for duloxetine, as its utilization increased steadily throughout its first full year of availability, after the patent protection of the branded version, Cymbalta®, expired in

December 2013. Lantus was the most-expensive traditional therapy drug, with a 2014 PMPY spend of \$77.17. Total trend for Lantus was 23.3%. Nexium was the second-most-expensive drug when ranked by PMPY spend. Despite the patent expiration for Nexium in 2014, generics for the brand were not approved until early 2015, due to regulatory problems. Utilization declined in six of the top 10 drugs, and two others saw moderate increases. Large double-digit increases in utilization and cost were observed for duloxetine and Levemir.

TOP 10 MEDICARE TRADITIONAL THERAPY DRUGS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL TRADITIONAL SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Lantus® (insulin glargine injection)	Diabetes	\$77.17	3.4%	-8.4%	31.7%	23.3%
2	Nexium® (esomeprazole magnesium)	Heartburn/Ulcer Disease	\$76.07	3.4%	-12.0%	12.7%	0.7%
3	Crestor® (rosuvastatin)	High Blood Cholesterol	\$70.25	3.1%	-1.4%	12.5%	11.1%
4	Abilify® (aripiprazole)	Mental/Neurological Disorders	\$51.17	2.3%	-1.8%	18.8%	16.9%
5	Advair Diskus® (fluticasone/salmeterol)	Asthma	\$50.23	2.2%	-11.2%	7.6%	-3.6%
6	Spiriva® (tiotropium)	COPD	\$47.27	2.1%	-4.5%	7.2%	2.7%
7	Namenda XR® (memantine extended release)	Mental/Neurological Disorders	\$44.52	2.0%	0.1%	16.3%	16.4%
8	Januvia® (sitagliptin)	Diabetes	\$40.88	1.8%	3.4%	17.7%	21.1%
9	duloxetine	Depression	\$34.09	1.5%	3,266.2%	-857.4%	2,408.8%
10	Levemir® (insulin detemir injection)	Diabetes	\$32.87	1.5%	60.5%	47.7%	108.2%

COMPARISON OF MEDICARE AND COMMERCIAL TREND: TRADITIONAL THERAPY CLASSES

MEDICARE TREND VERSUS COMMERCIAL TREND FOR THE TOP 10 MEDICARE TRADITIONAL THERAPY CLASSES

RANKED BY MEDICARE TREND

RANK	THERAPY CLASS	TREND		
		MEDICARE	COMMERCIAL	DIFFERENCE
1	Anticoagulants	60.2%	60.7%	-0.5%
2	Diabetes	26.4%	18.0%	8.4%
3	Pain/Inflammation	9.1%	16.0%	-6.9%
4	Mental/Neurological Disorders	4.2%	9.1%	-4.9%
5	Urinary Disorders	3.9%	-2.9%	6.8%
6	Asthma	2.4%	-14.9%	17.3%
7	High Blood Cholesterol	-1.0%	-6.8%	5.8%
8	Heartburn/Ulcer Disease	-4.1%	-10.6%	6.5%
9	High Blood Pressure/Heart Disease	-11.1%	-12.6%	1.5%
10	Depression	-18.7%	-18.4%	-0.3%
TOTAL		6.4%	6.4%	0.0%

Overall, the traditional therapy class trend for Medicare clients and for commercially insured clients was identical (6.4%). In addition, the trend for each of the 10 drugs in the class moved in the same direction for both groups of clients, with the exception of medications used to treat urinary disorders and asthma. The Medicare trend was moderately lower than the commercial trend for two classes – pain/inflammation and mental/neurological disorders – and was only marginally lower for depression and anticoagulants. The magnitude of trend for the diabetes therapy class was

greater for Medicare clients than for commercial clients because the prevalence of disease is higher in older individuals. Conversely, the increase in spend for asthma medications observed among Medicare beneficiaries (as opposed to the decline in spend seen for the commercially insured) is likely related to the utilization of some treatments classified as asthma medications to treat chronic obstructive pulmonary disease (COPD), which usually affects older populations.

MEDICARE: SPECIALTY THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 MEDICARE SPECIALTY THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Oncology	\$206.97	24.6%	12.6%	37.2%
2	Multiple Sclerosis	\$106.09	15.9%	12.1%	27.9%
3	Hepatitis C	\$106.02	145.2%	922.3%	1,067.5%
4	Inflammatory Conditions	\$86.95	12.8%	17.8%	30.7%
5	HIV	\$65.38	0.5%	7.8%	8.3%
6	Pulmonary Arterial Hypertension	\$34.66	13.4%	10.6%	24.0%
7	Miscellaneous Specialty Conditions	\$29.80	29.1%	27.4%	56.6%
8	Anticoagulants	\$14.31	-3.1%	-12.9%	-15.9%
9	Immune Deficiency	\$13.61	29.4%	-5.9%	23.6%
10	Blood Cell Deficiency	\$13.60	-1.7%	11.3%	9.6%
TOTAL SPECIALTY		\$724.94	11.6%	34.3%	45.9%

Ranked by per-member-per-year (PMPY) spend, the top three therapy classes together contributed **57.8%** of total specialty PMPY spend.

Among Medicare beneficiaries, overall trend for specialty medications was 45.9% in 2014, composed of an 11.6% increase in utilization and a 34.3% increase in unit cost. Ranked by PMPY spend, the top three therapy classes – oncology, multiple sclerosis and hepatitis C – together contributed 57.8% of total specialty PMPY spend. All but one of the top 10 therapy classes – anticoagulants – had significant increases in total spend in 2014. However, the key drivers of trend were by far the new drugs to treat hepatitis C. Therapies for blood cell deficiency and immune deficiency – the ninth and 10th ranked specialty classes, respectively – were unique to the top 10 list for Medicare beneficiaries when compared to the commercially insured and Medicaid populations, primarily because medications in the classes are used to treat conditions that more commonly affect older adults.

HIGHLIGHTS

- The increase in PMPY spend for cancer treatments continued to top that of other specialty medications. In 2014, PMPY spend increased 37.2%. Trend was driven by a substantial 24.6% increase in utilization and a 12.6% increase in unit cost. This utilization increase is likely the result of several factors, including the expansion of indications for several drugs; the continued development of newer, more targeted therapies; and an increase in the survival rates of patients living with cancer but continuing medication therapy. Nine new oncology agents were approved in 2014: Beleodaq™ (belinostat), Blincyto™ (blinatumomab), Cyramza® (ramucirumab), Keytruda® (pembrolizumab), Lynparza™ (olaparib), Opdivo® (nivolumab), Sylvant™ (siltuximab), Zydelig® (idelalisib) and Zykadia™ (ceritinib).
- Total trend for multiple sclerosis (MS) medications was 27.9%, due to increases in both utilization and unit cost. Tecfidera® (dimethyl fumarate), released in April 2013, continued to capture market share, likely because the oral administration it offers patients with MS is more convenient than that offered by injectables. Generics to Copaxone® (glatiramer), the market leader in this class, are expected to hit the market in September 2015, but the brand manufacturer is hoping to continue the shift of existing Copaxone users to a new, longer-acting formulation of the drug that has patent protection until 2030.
- Spend for inflammatory conditions increased 30.7%. Utilization increased substantially, but the main factor was the 17.8% increase in unit cost. One of the key treatments in this class is Xeljanz® (tofacitinib), the only oral disease modifying anti-rheumatic drug available. At the time of U.S. Food and Drug Administration (FDA) approval in 2012, its place in therapy was unclear due to questions concerning its safety profile. Now that longer-term safety and effectiveness data are available, Xeljanz has begun to capture Medicare market share from some more-established injectable treatments.
- Trend for medications used to treat blood cell deficiencies, some a temporary result of taking powerful chemotherapy agents, increased 9.6% in 2014, the unit-cost trend dampened somewhat by a 1.7% decrease in utilization. Many of the price tags for these branded medications increased in advance of biosimilars to drugs like Neupogen® (filgrastim), which could receive FDA approval in mid-2015, and Procrit® (epoetin alfa), which may be approved in the next two years.

Oncology trend was driven by a substantial **24.6%** increase in utilization and a **12.6%** increase in unit cost.

TOP 10 MEDICARE SPECIALTY DRUGS

For Medicare plans, the top 10 specialty drugs accounted for 44.4% of per-member-per-year (PMPY) spend for all specialty drugs in 2014. PMPY spend ranged from a low of \$17.66 for Avonex, an established multiple sclerosis treatment, to a high of \$66.22 for Sovaldi, one of three new hepatitis C treatments, all of which are in the top 10 list. Three cancer medications ranked in the top 10: Revlimid (the second-most-expensive specialty medication), Gleevec (the sixth) and Zytiga (the seventh). Even though they were launched in late 2013, Sovaldi and Olysio together contributed

11.7% of all Medicare specialty drug spend in 2014. Harvoni was only just launched in October 2014, and in that short time contributed 2.5% of specialty spend. Olysio had the largest increase in total PMPY spend (26,028.7%), partly driven by increased utilization after the market availability of the drug reached a full calendar year. Aside from the hepatitis C medications, the largest increase in utilization and total spend was observed for Zytiga, an oncology medication indicated for the treatment of metastatic prostate cancer. The incidence of prostate cancer rises substantially with age.²⁶

TOP 10 MEDICARE SPECIALTY THERAPY DRUGS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL SPECIALTY SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Sovaldi® (sofosbuvir)	Hepatitis C	\$66.22	9.1%	15,624.4%	476.7%	16,101.1%
2	Revlimid® (lenalidomide)	Oncology	\$47.78	6.6%	14.1%	6.3%	20.3%
3	Copaxone® (glatiramer)	Multiple Sclerosis	\$36.91	5.1%	-2.2%	10.2%	8.0%
4	Enbrel® (etanercept)	Inflammatory Conditions	\$33.46	4.6%	3.4%	17.0%	20.4%
5	Humira® (adalimumab)	Inflammatory Conditions	\$33.17	4.6%	6.4%	17.6%	24.0%
6	Gleevec® (imatinib)	Oncology	\$29.31	4.0%	6.0%	20.4%	26.4%
7	Zytiga® (abiraterone)	Oncology	\$21.05	2.9%	39.9%	14.2%	54.1%
8	Olysio® (simeprevir)	Hepatitis C	\$18.60	2.6%	25,964.2%	64.5%	26,028.7%
9	Harvoni® (ledipasvir/sofosbuvir)	Hepatitis C	\$18.01	2.5%	N/A	N/A	N/A
10	Avonex® (interferon beta 1-a)	Multiple Sclerosis	\$17.66	2.4%	-4.4%	11.6%	7.2%

COMPARISON OF MEDICARE AND COMMERCIAL TREND: SPECIALTY THERAPY CLASSES

MEDICARE TREND VERSUS COMMERCIAL TREND FOR THE TOP 10 MEDICARE SPECIALTY THERAPY CLASSES

RANKED BY MEDICARE TREND

RANK	THERAPY CLASS	TREND		
		MEDICARE	COMMERCIAL	DIFFERENCE
1	Hepatitis C	1,067.5%	742.6%	324.9%
2	Miscellaneous Specialty Conditions	56.6%	35.6%	21.0%
3	Oncology	37.2%	20.7%	16.5%
4	Inflammatory Conditions	30.7%	24.3%	6.4%
5	Multiple Sclerosis	27.9%	12.9%	15.0%
6	Pulmonary Arterial Hypertension	24.0%	13.8%	10.2%
7	Immune Deficiency	23.6%	21.2%	2.4%
8	Blood Cell Deficiency	9.6%	0.9%	8.7%
9	HIV	8.3%	14.8%	-6.5%
10	Anticoagulants	-15.9%	-14.1%	-1.8%
	TOTAL SPECIALTY	45.9%	30.9%	15.0%

Overall, the trend for specialty therapy classes experienced by Medicare clients (45.9%) was significantly higher than that experienced by commercially insured clients (30.9%), related to differences in disease prevalence and drug utilization for older patients versus younger ones. In each therapy class, specialty drug trend for Medicare and commercially insured clients moved in the same direction. HIV treatments and anticoagulants were the only therapy classes in the top 10 for which the trend for Medicare beneficiaries was lower than that for their commercially insured counterparts.

Although the number of Medicare beneficiaries with HIV has risen dramatically,²⁷ new infections are still more likely to be diagnosed in individuals under, rather than over, the age of 55.²⁸ Newer anticoagulants classified as traditional drugs because of their ease of administration captured additional market share among Medicare beneficiaries, who are much older, on average, than their commercially insured counterparts and therefore more likely to use anticoagulant therapy.



MEDICAID

MEDICAID YEAR IN REVIEW

8.7 million adults and children were added to the Medicaid program in 2014, bringing the number of Medicaid beneficiaries nationwide to **67.9 million**.

During 2014, multiple factors affected trend for health plans that manage pharmacy benefits for Medicaid beneficiaries, including: the expansion of Medicaid coverage and subsequent increase in Medicaid beneficiaries that followed implementation of the 2010 Affordable Care Act (ACA); changes to the Medicaid program by state legislatures, and clinical advances and subsequent treatment guideline updates.

Expansion of Medicaid Coverage

In support of its goal of decreasing the number of uninsured Americans and making health insurance more affordable, the ACA gave states the option of receiving federal funds to offset the costs of raising the Medicaid threshold to households with incomes less than 138% of the federal poverty level. The legislatures in 25 states, along with the government of the District of Columbia, chose to raise eligibility thresholds in 2014. In addition, the ACA extended Medicaid coverage to childless adults, who previously had not been eligible for the program.²⁹ Consequently, we saw the number of Medicaid beneficiaries over age 19 grow from 40.2% in 2013 to 44.2% in 2014. Also contributing to growth in the Medicaid population was what has been called “the woodwork effect.” As some individuals were applying for health insurance coverage through the federal exchange or one of the 25 state exchanges, they discovered that they were eligible for Medicaid coverage and thus were “drawn out of the woodwork.” As a result, 8.7 million adults and children were added to the Medicaid program in 2014, bringing the number of Medicaid beneficiaries nationwide to 67.9 million.³⁰

With their numbers of Medicaid beneficiaries increased dramatically but unevenly, states took varying approaches to managing the Medicaid pharmacy benefit. Many that chose Medicaid expansion had previously used some form of managed care to control the operational and medical costs of managing enrollee benefits. A few states implemented managed care tools for their expansion population, using a different care model than they had previously utilized. This resulted in various levels of trend management success across states.

State Legislation

In 2014, some states enacted legislation that changed the requirements for the management of prescription drug benefits, thereby limiting the strategies available to Medicaid plan sponsors to control the cost and utilization of the pharmacy benefit.

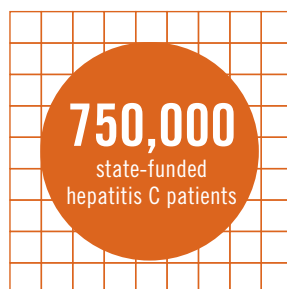
As part of Florida's statewide expansion of managed care Medicaid, that state now requires all participating health plans to use a state-mandated formulary for the first year of a contract. The state of Washington took a different approach, enacting regulations that require health plans to maintain an "open" formulary status for patients who continue to fill prescriptions for previously prescribed atypical antipsychotics, antidepressants and medications for attention deficit hyperactivity disorder (ADHD).

Meanwhile, New York made changes to its "Prescriber Prevails" program; implemented in 2012, the program allows a prescriber's professional judgment to prevail in the prior-authorization process, thereby allowing some patients to bypass the prior authorization process usually required for some drugs. Originally focused on medically necessary atypical antipsychotics, the New York program was expanded in 2013 to apply to other drug categories, including transplant medications, antidepressants, specialty inflammatory condition therapies and anti-seizure medications. In 2014, New York continued to add medications to this list, which affects the ability of Medicaid payers to manage costs.

Clinical Advances

The largest impact on trend for Medicaid plans in 2014 stemmed from U.S. Food and Drug Administration (FDA) approval of three expensive new oral hepatitis C treatments: Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir). Treatment with these specialty drugs is one of the most expensive therapeutic regimens available, and the cost for a course of therapy can reach as high as \$150,000. With more than 750,000 patients with chronic hepatitis C receiving state-funded healthcare through either Medicaid or the prison system, the burden of paying for the cost of these hepatitis C treatment regimens falls disproportionately on state budgets, as opposed to commercial insurance plan budgets.

Based on the pricing strategy offered by drug manufacturers when Sovaldi first launched, Express Scripts projected that states would spend a total of more than \$55.2 billion if they provided all these hepatitis C patients with one of the newest therapy regimens that included Sovaldi. Express Scripts estimated that five states would be faced with the highest spend: California, Texas, Florida, New York and Illinois.



Because Sovaldi was released in late 2013, after most state Medicaid agencies had calculated their capitation rates for managed care organizations for 2014, those rates did not take into account the cost of these new, expensive treatment regimens. Neither had most state Medicaid agencies predicted the impact that paying for these therapies would have on their budgets. This concern was raised by state Medicaid agencies in 2014, as they tried to create treatment guidelines while facing high demand for these products and large financial outlays.

The concerns of state agencies were warranted. Hepatitis C medications had a trend of 317.2% for 2014 – a higher trend than that for any other therapy class. In addition, the per-member-per-year (PMPY) spend for this therapy class, at \$55.02, was higher than the spend for all but three of the top 10 therapy classes across both traditional and specialty drugs – even though the prevalence of use for hepatitis C medications was dramatically lower than that for other medications in the top 10 classes. This dramatic increase in spend is reminiscent of the staggering increases in price for HIV/AIDS medications that were seen in the early 2000s, when the new subclass of antiretroviral therapy became the standard of care for HIV/AIDS.

The largest impact on trend for Medicaid plans in 2014 stemmed from FDA approval of three expensive new oral hepatitis C treatments: Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir).

TREND MANAGEMENT STRATEGIES

Tighter Specialty Drug Management and Accredo

While Express Scripts and our clients continue to advocate for more sustainable and fair drug pricing, there are important strategies that Medicaid plans can implement to ensure the most appropriate use of these medications. One recommended strategy is tighter management for high-priced specialty medications to help ensure that the right patients receive the right treatments. This tighter management can occur through updated prior authorization and treatment guidelines, including the use of exclusive specialty drug distribution channels like Accredo, the Express Scripts specialty pharmacy.

We have seen state Medicaid agencies implement various guidelines, such as making viral load testing a requirement for continued authorization of medication; split-fill dispensing, allowing only 14-day dispensing; evaluation of illegal drug use; and retreatment limits. We encourage health plans to review and consider the approaches taken in the marketplace as they create their own guidelines.

Encouraging the use of exclusive specialty drug distribution channels like Accredo – rather than retail pharmacies – can dramatically improve medication adherence. For example, among patients with cancer, our specialized care improved medication adherence by 16 percentage points; among patients with multiple sclerosis, adherence improved 32 percentage points.

Medication adherence is critically important for patients with conditions such as hepatitis C – from the standpoint of both the high costs of the newer therapies being used to treat the condition and concerns about clinical effectiveness and possible future complications due to nonadherence. A recent analysis underlines the importance of Accredo's programs for patients with hepatitis C. It found that hepatitis C patients who do not experience the unique clinical model available through Accredo are nearly twice as likely to fail their therapy.

Smart Formulary Management

Another strategy we recommend is smart formulary management. Today, most therapy classes offer more drug choices than ever. Yet many prescription drugs that cost more deliver no additional health benefit. Smart formulary management is vital to offering a sustainable pharmacy benefit that preserves patient access and choice while helping payers obtain fair and affordable pricing. Express Scripts modeled this type of smart formulary management by excluding a handful of “me-too” products from the Express Scripts National Preferred Formulary. This step created the necessary leverage to negotiate more effectively with manufacturers and ultimately achieve lower drug prices for the clients and patients we serve. To ensure needed access, in the rare instance when a patient has a medical need for an off-formulary drug, we have created a pathway for the excluded drug to be covered for the patient.

Smart formulary management can also include preference for one product over another when the products are clinically equivalent. Throughout 2014, Express Scripts was largely critical of a recent trend of drug manufacturers bringing to market products that, although innovative, were priced at levels that were so high that they were unsustainable for payers. For example, the \$84,000 treatment cost for the hepatitis C drug, Sovaldi (sofosbuvir), threatened to bankrupt both private and public plan sponsors around the United States. After a year-long

campaign advocating for fairer drug pricing, Express Scripts announced in December a new agreement with AbbVie, makers of the new hepatitis C medication, Viekira Pak™ (ombitasvir/paritaprevir/ritonavir co-packaged with dasabuvir). The unprecedented arrangement expands both payer affordability and patient access. The cost to cure is now low enough that plan sponsors can afford to treat all hepatitis C patients with genotype 1, not just the sickest.

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Clinical Solutions

An additional strategy that health plans can implement is Express Scripts clinical solutions that align pharmacists, physicians, patients and case managers to help drive optimal performance against both pharmacy and medical measures. The clinically specialized Therapeutic Resource Centers (TRCs) of the Express Scripts Pharmacy and Accredo Specialty Pharmacies deliver superior treatment outcomes and cost-effectiveness by supporting patients through the challenges of complex and costly diseases. Our specialist pharmacists and nurses each receive clinically specialized training in one disease state, and the work they do focuses almost exclusively on that clinical condition. This specialized expertise and commitment enables an optimal patient experience and ensures the highest performance in pharmacy safety, improved medication adherence and closing gaps in care. With their highly specialized knowledge of the complex disease states and complicated treatment protocols they manage, these TRC pharmacists and nurses often have more experience in rare conditions than some of the physicians who prescribe the treatments.

Because each Medicaid health plan's needs are unique, our menu of available programs is designed to meet varying needs – from ScreenRx® for predictive modeling and tailored interventions to drive adherence; to RationalMed® using proprietary clinical analysis of prescription, medical and lab data to identify safety risks; to targeted diabetes treatment initiatives supporting physician prescribing best practices.

A LOOK AT MEDICAID OVERALL DRUG TREND FOR 2014

Overall trend for Medicaid plans was 10.2% in 2014, due primarily to a 10.7% increase in unit cost. Utilization was marginally negative (-0.5%), reflecting the influx of new, adult beneficiaries less likely to use medications for chronic conditions. Because the number of prescriptions remained similar from 2013 to 2014, but the number of beneficiaries across which to divide the costs grew, a decrease in utilization was reflected. Overall per-member-per-year (PMPY) spend was \$882.43 (vs. \$800.65 in 2013).

Traditional trend was 2.8% – far below that observed in either the commercially insured or Medicare populations – reflecting a 3.2% increase in unit cost, offset somewhat by a 0.5% decrease in utilization. Spend for traditional medications contributed 72.2% of total PMPY spend in 2014 – a lower share than the 77.7% observed in 2013. The decrease in share of spend for traditional medications was due to the impact of the new, expensive specialty medications, Sovaldi, Olysio and Harvoni among them, which contributed significantly to a 35.8% increase in PMPY spend for specialty drugs in 2014 – three times that in 2013.

PMPY spend and trend varied across age groups. For beneficiaries age 20 to 34, total trend was -2.5% – the drop due largely to the increase in the number of younger adult beneficiaries in this age range. PMPY spend for these beneficiaries was \$828.78. As in 2013, PMPY spend for beneficiaries age 35 to 64, at \$2,222.82, was higher than that for all other age groups. The 4.1% trend for this age group was driven entirely by an increase in unit cost for specialty medications. The highest trend, 12.4%, was among beneficiaries age 65 and older, again driven by increased unit costs for specialty medications.

COMPONENTS OF MEDICAID TREND

2014

	TREND			
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	\$637.42	-0.5%	3.2%	2.8%
Specialty	\$245.01	-0.9%	36.7%	35.8%
TOTAL OVERALL	\$882.43	-0.5%	10.7%	10.2%

January-December 2014 compared to same period in 2013

AGES 0 TO 19, 2014

	TREND			
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	\$266.52	-1.8%	7.2%	5.3%
Specialty	\$56.49	0.2%	11.6%	11.7%
TOTAL OVERALL	\$323.01	-1.8%	8.2%	6.4%

January-December 2014 compared to same period in 2013

AGES 20 TO 34, 2014

	TREND			
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	\$583.57	-9.6%	1.1%	-8.6%
Specialty	\$245.22	-8.7%	24.6%	16.0%
TOTAL OVERALL	\$828.78	-9.6%	7.1%	-2.5%

January-December 2014 compared to same period in 2013

AGES 35 TO 64, 2014

	TREND			
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	\$1,534.93	-7.5%	2.6%	-4.9%
Specialty	\$687.89	-9.9%	41.8%	31.9%
TOTAL OVERALL	\$2,222.82	-7.5%	11.6%	4.1%

January-December 2014 compared to same period in 2013

AGES 65 AND OLDER, 2014

	TREND			
	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
Traditional	\$680.89	-2.1%	5.9%	3.8%
Specialty	\$180.94	-2.4%	65.6%	63.2%
TOTAL OVERALL	\$861.83	-2.1%	14.5%	12.4%

January-December 2014 compared to same period in 2013

MEDICAID: TRADITIONAL THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 MEDICAID TRADITIONAL THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Diabetes	\$106.13	1.4%	17.0%	18.4%
2	Mental/Neurological Disorders	\$81.60	-7.2%	7.0%	-0.2%
3	Asthma	\$67.95	-5.1%	1.1%	-4.1%
4	Pain/Inflammation	\$52.38	-3.2%	12.3%	9.1%
5	Attention Disorders	\$44.05	-4.1%	5.1%	1.0%
6	Seizures	\$22.15	-3.0%	5.2%	2.1%
7	Infections	\$20.82	-6.6%	2.2%	-4.4%
8	Chemical Dependence	\$19.29	6.4%	-14.0%	-7.6%
9	Depression	\$18.10	5.7%	-22.1%	-16.4%
10	High Blood Pressure/Heart Disease	\$17.24	4.2%	-9.6%	-5.5%
TOTAL TRADITIONAL		\$637.42	-0.5%	3.2%	2.8%

Ranked by per-member-per-year (PMPY) spend, the top 10 traditional therapy classes accounted for **70.6%** of Medicaid traditional spend.

Ranked by PMPY spend, the top 10 traditional therapy classes accounted for 70.6% of Medicaid traditional spend. For the second year in a row, medications used to treat diabetes were the most-expensive traditional therapy class, contributing 16.6% of overall Medicaid traditional drug spend. Six of the top 10 traditional therapy classes had negative total trend, with the largest decline seen in spend for antidepressants.

HIGHLIGHTS

- PMPY spend for diabetes in 2014 was higher than that for any other traditional therapy class. Total trend for diabetes medications was 18.4%, resulting mainly from a significant increase in unit cost (17.0%). Brand inflation for insulin therapies contributed heavily to the unit-cost increase. For example, the unit cost for Lantus® (insulin glargine [rDNA origin]) increased 32.8% – likely in anticipation of biosimilar insulin glargine expected in 2017 and probable competition from ultra-long acting insulins that are in the pipeline for approval in the next few years. Costs for other insulins, like Humalog® (insulin lispro [rDNA origin]), also went up.
- Despite a 3.2% decrease in utilization, trend for pain/inflammation treatments was 9.1% in 2014. The class, which includes a variety of treatments for pain – including not only opioids like hydrocodone, but also GABA receptor agonists like gabapentin and NSAIDs like naproxen – is almost exclusively generic; the generic fill rate (GFR) for the class was 97.5% in 2014. However, market dynamics in 2014 led to double-digit increases in unit costs for two of the most commonly used treatments among Medicaid beneficiaries, lidocaine and oxycodone/acetaminophen.
- Total trend for medications used to treat attention disorders was a modest 1.0%, mostly as a result of a 4.1% decrease in utilization. This decrease may be partly related to increased scrutiny of medications for attention deficit hyperactivity disorder (ADHD) that are used by Medicaid beneficiaries.³¹ The decrease in utilization of therapies for attention deficit – which are prescribed most often for children – may also be attributable to age shifts in the Medicaid population following implementation of the ACA.
- Although utilization of depression medications increased 5.7% in 2014, the 22.1% decrease in unit cost led the class to the largest negative total trend (-16.4%) among the top 10 traditional therapy classes. The biggest reason for the decline in the unit cost was an increase in the GFR from 94.0% in 2013 to 98.6% in 2014. One of the last remaining brand serotonin norepinephrine reuptake inhibitors (SNRIs), Cymbalta® (duloxetine), lost patent protection at the end of 2013, with the result that all of the top 10 most commonly used antidepressants in 2014 were generics.

Brand inflation for insulin therapies contributed heavily to the **17.0%** increase in unit cost for diabetes treatments.

TOP 10 MEDICAID TRADITIONAL DRUGS

Nine of the top 10 traditional drugs used by Medicaid beneficiaries in 2014 were brands, which contributed 25.8% of per-member-per-year (PMPY) spend for all traditional therapy drugs. The only generic medication in the top 10, methylphenidate, is used to treat attention deficit hyperactivity disorder (ADHD). As in 2013, the Medicaid traditional therapy drug with the highest PMPY spend was the antipsychotic Abilify. Total trend was 6.0% for Abilify, as the decrease in utilization was offset by an increase in unit cost; the increase in unit cost likely occurred in anticipation of the expiration of the drug's patent in April 2015. The highest trend, for Symbicort (53.2%) was driven mostly by a 42.7% increase in utilization.

As in 2013, the Medicaid traditional therapy drug with the highest PMPY spend was the antipsychotic Abilify. Total trend was **6.0%** for Abilify.

TOP 10 MEDICAID TRADITIONAL THERAPY PRODUCTS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL TRADITIONAL SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Abilify® (aripiprazole)	Mental/Neurological Disorders	\$40.99	6.4%	-11.3%	17.2%	6.0%
2	Lantus® (insulin glargine injection)	Diabetes	\$27.30	4.3%	2.5%	32.8%	35.3%
3	Humalog® (insulin lispro injection)	Diabetes	\$18.77	2.9%	19.1%	25.5%	44.6%
4	OneTouch Ultra® Test Strips	Diabetes	\$16.93	2.7%	-2.5%	2.0%	-0.5%
5	Suboxone® (buprenorphine/naloxone)	Chemical Dependence	\$14.08	2.2%	-15.6%	-4.9%	-20.5%
6	Symbicort® (budesonide/formoterol)	Asthma	\$13.10	2.1%	42.7%	10.5%	53.2%
7	methylphenidate extended release	Attention Disorders	\$12.24	1.9%	-3.9%	-1.0%	-4.9%
8	Ventolin® HFA (albuterol)	Asthma	\$11.95	1.9%	4.2%	5.6%	9.8%
9	Spiriva® (tiotropium)	Chronic Obstructive Pulmonary Disease	\$10.86	1.7%	-3.0%	7.2%	4.1%
10	Advair Diskus® (fluticasone/salmeterol)	Asthma	\$10.27	1.6%	-34.0%	6.3%	-27.7%

MEDICAID: SPECIALTY THERAPY CLASSES AND INSIGHTS

COMPONENTS OF TREND FOR THE TOP 10 MEDICAID SPECIALTY THERAPY CLASSES

RANKED BY 2014 PMPY SPEND

RANK	THERAPY CLASS	PMPY SPEND	TREND		
			UTILIZATION	UNIT COST	TOTAL
1	Hepatitis C	\$55.02	4.6%	317.2%	321.8%
2	HIV	\$48.28	0.7%	10.3%	11.0%
3	Inflammatory Conditions	\$30.63	14.4%	21.5%	35.9%
4	Oncology	\$25.50	11.2%	11.8%	23.0%
5	Multiple Sclerosis	\$24.52	0.2%	11.3%	11.5%
6	Miscellaneous Specialty Conditions	\$9.66	39.4%	26.6%	66.0%
7	Growth Deficiency	\$8.20	-9.2%	4.2%	-5.0%
8	Cystic Fibrosis	\$7.29	1.7%	6.7%	8.5%
9	Pulmonary Arterial Hypertension	\$5.60	7.5%	-2.8%	4.8%
10	Anticoagulants	\$4.92	-2.0%	-13.2%	-15.2%
TOTAL SPECIALTY		\$245.01	-0.9%	36.7%	35.8%

Hepatitis C medications contributed
65.0% of the total increase in
specialty spend.

Overall trend for specialty medications used by Medicaid beneficiaries was 35.8% in 2014, fueled by the significant increase in unit cost related to the launch of three new hepatitis C treatments – Sovaldi® (sofosbuvir), Olysio® (simeprevir) and Harvoni® (ledipasvir/sofosbuvir). Hepatitis C medications contributed 65.0% of the total increase in specialty spend. Accordingly, hepatitis C medications were the most-expensive Medicaid specialty therapy class when ranked by PMPY spend. The top three therapy classes – hepatitis C, HIV and inflammatory conditions – together contributed 54.7% of total specialty PMPY spend. Two of the top 10 therapy classes – growth deficiency and anticoagulants – had negative total trend in 2014. Only pulmonary arterial hypertension and anticoagulants had a decrease in unit cost from 2013 to 2014.

HIGHLIGHTS

- Total trend for HIV medications was 11.0%, almost exclusively from an increase in unit cost. Although the wave of patent expirations in this class continues, generic availability may not reduce the cost of HIV therapy because a constantly changing pipeline is needed to address mutations in virus strains that cause resistance to drugs. Additionally, older HIV drugs that may have generic equivalents must be taken several times a day in combination with other drugs, and newer treatments that combine multiple medications into one-dose form offer more convenient dosing regimens. For example, Stribild®(elvitegravir/cobicistat/emtricitabine/tenofovir) is taken only once a day; and although Tivicay® (dolutegravir), another relatively recent FDA approval, must be taken with other drugs, dosage is only twice a day. Both brand medications gained significant market share in 2014, but both come with much higher price tags than generics.
- A 9.2% decrease in utilization was offset by a 4.2% increase in unit cost, resulting in a -5.0% trend for growth deficiency treatments among Medicaid beneficiaries. Growth hormone treatments are another class of medications that is primarily used by children, so a shift in the age structure of the Medicaid population following the expansion of the Medicaid program in some states could be contributing to the decrease in utilization.
- Both the cost and the utilization of cystic fibrosis (CF) treatments increased in 2014. However, utilization of Kalydeco® (ivacaftor), the first drug to treat the underlying cause of disease in patients with a rare form of CF, dropped 6.7%. The annual price tag for Kalydeco, an oral drug, can exceed \$300,000. A new drug, lumacaftor, is in development; if approved, it will be taken in combination with Kalydeco to treat underlying genetic mutations that cause the most common form of CF.
- Medicaid spend for specialty anticoagulant medications continued to decline, spurred by a 13.2% decrease in unit cost. The 99.6% generic fill rate (GFR) and its associated lower costs far outweighed the 2014 price increases observed for the few remaining brands in the class.

Utilization of Kalydeco® (ivacaftor), the first drug to treat the underlying cause of disease in patients with a rare form of CF, dropped **6.7%**.

THE TOP 10 MEDICAID SPECIALTY DRUGS

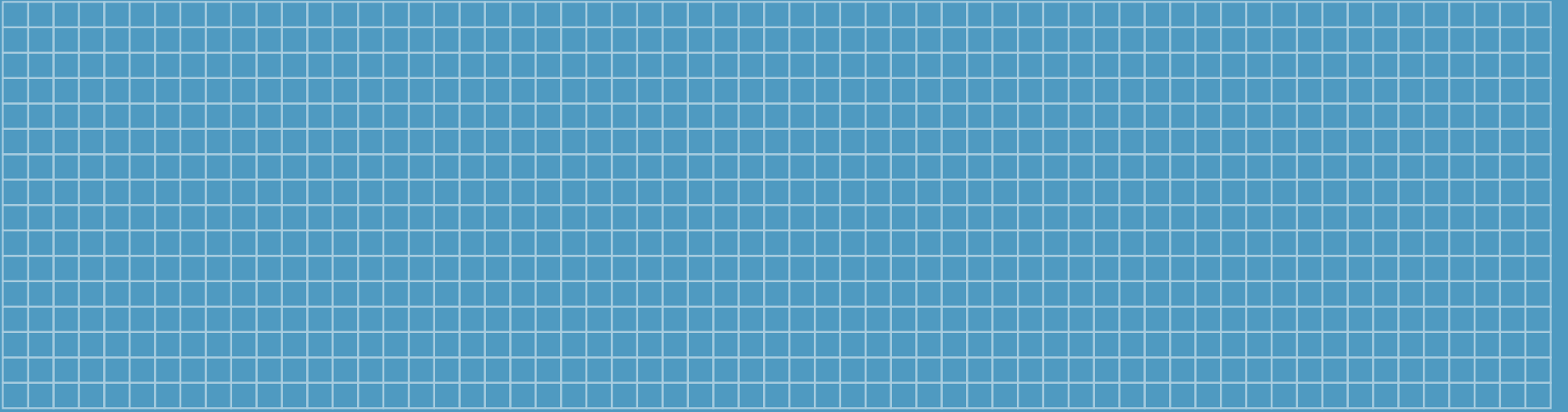
For Medicaid plans, the top 10 specialty drugs accounted for 44.5% of per-member-per-year (PMPY) spend for all specialty drugs in 2014. PMPY spend ranged from \$43.13 for Sovaldi to \$4.32 for generic enoxaparin. Sovaldi captured 17.6% of PMPY spend for all specialty drugs in 2014. The PMPY spend for Sovaldi was also more than triple the PMPY spend for the second-most-expensive drug, Humira, which had almost three times the utilization Sovaldi did in 2014. Three HIV medications captured spots in the top 10: Atripla, Truvada and Viread, which ranked fourth, fifth and seventh, respectively. Aside from Sovaldi, the oral MS treatment, Tecfidera, had the highest trend (247.7%), driven by a triple-digit increase in utilization, likely spurred by the added convenience of administration for an oral medication over an injectable treatment.

PMPY spend ranged from **\$43.13** for Sovaldi to **\$4.32** for generic enoxaparin.

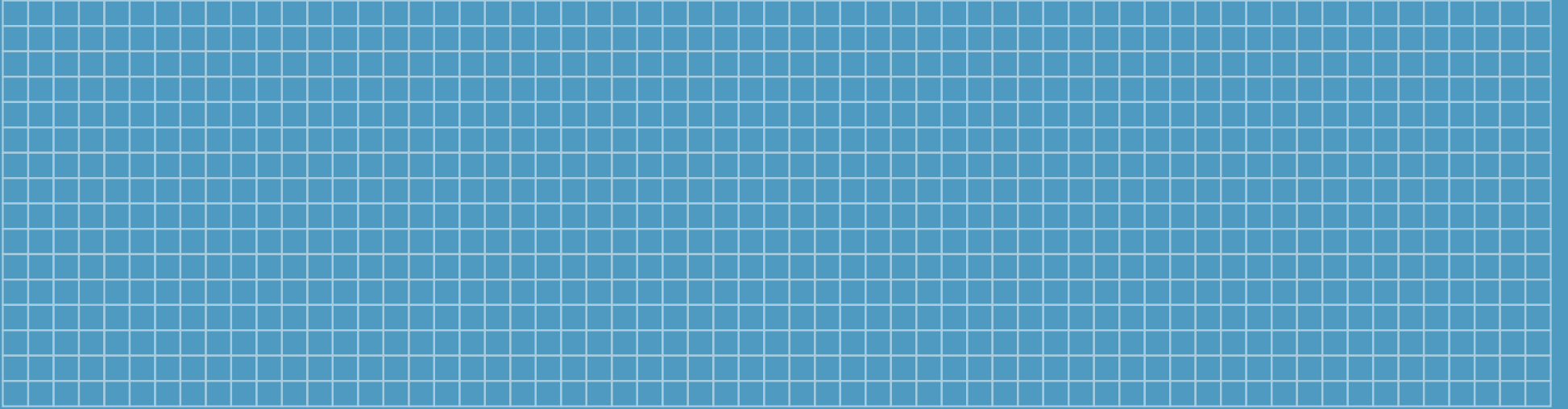
TOP 10 MEDICAID SPECIALTY THERAPY DRUGS

RANKED BY 2014 PMPY SPEND

RANK	DRUG NAME	THERAPY CLASS	PMPY SPEND	% OF TOTAL SPECIALTY SPEND	TREND		
					UTILIZATION	UNIT COST	TOTAL
1	Sovaldi® (sofosbuvir)	Hepatitis C	\$43.13	17.6%	33131.0%	-503.2%	32627.8%
2	Humira® (adalimumab)	Inflammatory Conditions	\$12.78	5.2%	11.4%	19.9%	31.3%
3	Enbrel® (etanercept)	Inflammatory Conditions	\$9.35	3.8%	10.4%	18.7%	29.2%
4	Atripla® (efavirenz/emtricitabine/tenofovir)	HIV	\$8.82	3.6%	-7.4%	7.0%	-0.3%
5	Truvada® (emtricitabine/tenofovir)	HIV	\$8.77	3.6%	-0.5%	4.3%	3.8%
6	Copaxone® (glatiramer)	Multiple Sclerosis	\$6.51	2.7%	-11.7%	9.0%	-2.7%
7	Viread® (tenofovir)	HIV	\$5.58	2.3%	-2.2%	4.0%	1.8%
8	Tecfidera® (dimethyl fumarate)	Multiple Sclerosis	\$5.19	2.1%	216.3%	31.4%	247.7%
9	Avonex® (interferon beta 1-a)	Multiple Sclerosis	\$4.61	1.9%	-28.4%	8.3%	-20.1%
10	enoxaparin	Anticoagulants	\$4.32	1.8%	1.2%	-13.0%	-11.7%



APPENDIX



THE DRUG TREND REPORT

METHODOLOGY

Prescription drug use for members with drug coverage provided by Express Scripts plan sponsors³² was analyzed for the Drug Trend Report. The plan sponsors providing the pharmacy benefit paid at least some portion of the cost for the prescriptions dispensed to their members, providing what is known as a funded benefit.

Both traditional and specialty drugs are included. Specialty medications include injectable and noninjectable drugs that are typically used to treat chronic, complex conditions and may have one or more of the following qualities: frequent dosing adjustments or intensive clinical monitoring; intensive patient training and compliance assistance; limited distribution; and specialized handling or administration. Nonprescription medications (with the exception of diabetic supplies billed under the pharmacy benefit) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings, or billed under the medical benefit are not included.

Trend and other measures are calculated separately for those members with commercial insurance coverage, for Medicaid recipients and for Medicare beneficiaries receiving prescription benefits through Employer Group Waiver Plans (EGWPs), managed Medicare Prescription Drug Plans (PDPs) or Medicare Advantage Prescription Drug Plans (MAPDs). Members used Express Scripts for retail and home delivery pharmacy services; they used Accredo, the Express Scripts specialty pharmacies, for specialty drug prescriptions.

Total trend measures the rate of change in plan costs, which include ingredient costs, taxes, dispensing fees and administrative fees. Rebates are not included as a component of cost. Total trend comprises utilization trend and unit cost trend. Utilization trend is defined as the rate of change in total days' supply of medication per member, across prescriptions. Unit cost trend is defined as the rate of change in costs due to inflation, discounts, drug mix and member cost share. Utilization and cost are determined on a per-member-per-year (PMPY) basis. Metrics are calculated by dividing totals by the total number of member-months, which is determined by adding the number of months of eligibility for all members in the sample.

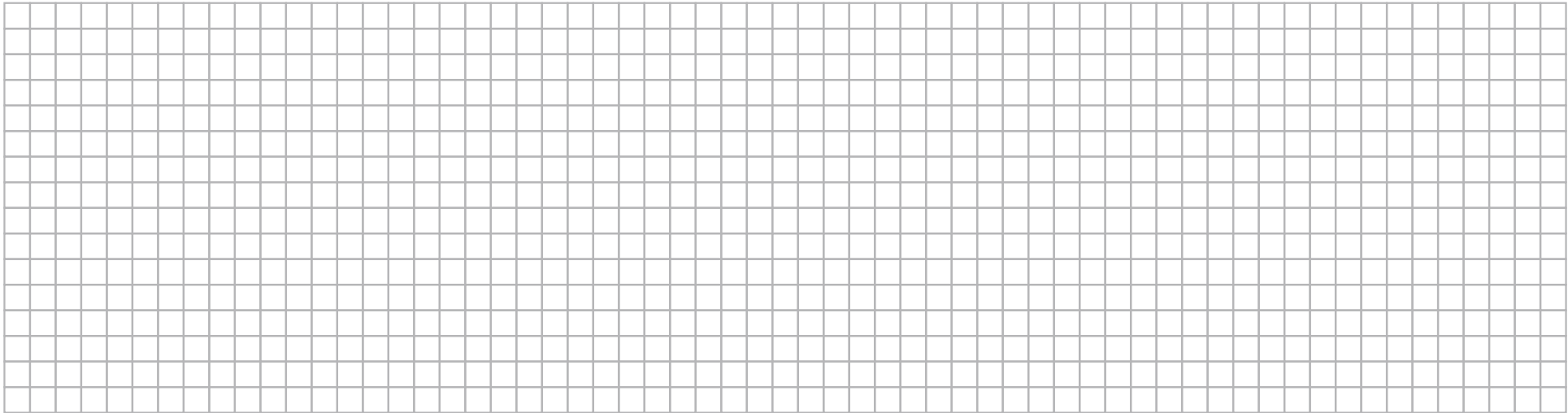
The Express Scripts Prescription Price Index (PPI) measures inflation in prescription drug prices by monitoring changes in consumer prices for a fixed market basket of commonly used prescription drugs. Separate market baskets are defined for brand drugs and for generic drugs, and are based on the top 80% of utilized drugs.

Please Note: Although up to nine decimal places were allowed in making all calculations, in most cases the results were rounded down to one or two decimals for easier reading. Therefore, dollar and percentage calculations may be slightly off due to rounding.

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32. Plan sponsors were excluded if they were not Express Scripts clients in both periods, if they had less than 12 months of claims data in either period, if they had retail-only benefits, if they had 100% or 0% copayment benefits, if they had eligibility shifts exceeding 20% for commercial plans (eligibility shifts exceeding 50% for Medicare and Medicaid plans), or if they were contractually prohibited from inclusion. Individual members might be covered, and thus included, for only a portion of the time periods of interest.



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